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PERKIN AND KIPPING'S ORGANIC CHEMISTRY

BY

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PART II. .

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CONTENTS OF PART II.

	PAGE
CHAPTER XX.—PRODUCTION, PURIFICATION, AND PROPERTIES OF BENZENE	325
CHAPTER XXI.—CONSTITUTION OF BENZENE, AND ISOMERISM OF BENZENE DERIVATIVES	333
The Orientation of Benzene Derivatives	343
CHAPTER XXII.—GENERAL PROPERTIES OF AROMATIC COM- POUNDS	351
Classification of Organic Compounds	351
General Character of Aromatic Compounds	353
CHAPTER XXIII.—HOMOLOGUES OF BENZENE AND OTHER HYDRO- CARBONS	360
Toluene—Xylenes—Ethylbenzene—Mesitylene—Cymene	365
Diphenyl—Diphenylmethane—Triphenylmethane	369
CHAPTER XXIV.—HALOGEN DERIVATIVES OF BENZENE AND OF ITS HOMOLOGUES	371
Chlorobenzene—Bromobenzene—Iodobenzene—Chlorotoluenes —Benzyl Chloride	375
CHAPTER XXV.—NITRO COMPOUNDS	380
Nitrobenzene—Dinitrobenzenes—Nitrotoluenes	383
CHAPTER XXVI.—AMINO-COMPOUNDS AND AMINES	386
Aniline and its Derivatives	390
Homologues of Aniline	394
Alkylanilines	395
Diphenylamine and Triphenylamine	398
Aromatic Amines—Benzylamine	399
CHAPTER XXVII.—DIAZONIUM-SALTS AND RELATED COMPOUNDS	400
Constitution of Diazonium Salts	404
Hydrazines and Hydrazones—Phenylhydrazine	405
Diazoamino- and Azo Compounds	408
Diazo Derivatives of Aliphatic Compounds	412
CHAPTER XXVIII.—SULPHONIC ACIDS AND THEIR DERIVATIVES	415
Benzenesulphonic Acid	418
Sulphanilic Acid.	419

	PAGE
CHAPTER XXIX — PHENOLS	420
Monohydric Phenols—Phenol, Picric Acid, Cresols	425
Dihydric Phenols—Catechol, Resorcinol, Quinol	430
Trihydric Phenols—Pyrogallol, Phloroglucinol	432
Thiophenols and Sulphides	434
CHAPTER XXX — AROMATIC ALCOHOLS, ALDEHYDES, KETONES, AND QUINONES	435
Alcohols—Benzyl Alcohol	435
Aldehydes—Benzaldehyde	437
Phenolic or Hydroxy-Aldehydes—Salicylaldehyde	441
Ketones—Acetophenone—Benzophenone	443
Quinones—Quinone— <i>o</i> -Benzoquinone	445
CHAPTER XXXI.—CARBOXYLIC ACIDS	448
Benzoic Acid—Benzoyl Chloride—Benzoic Anhydride—Benz- amide—Benzonitrile	451
Substitution Products of Benzoic Acid	454
Anthranilic Acid—Toluic Acids	455
Dicarboxylic Acids—Phthalic Acid, Phthalic Anhydride, Phthalimide	456
Isophthalic Acid, Terephthalic Acid	459
Phenylacetic Acid, Phenylpropionic Acid, and Derivatives	460
Cinnamic Acid and Related Compounds	463
CHAPTER XXXII. — PHENOLIC AND HYDROXY-CARBOXYLIC ACIDS	466
Salicylic Acid—Anisic Acid—Gallic Acid—Tannin	469
Mandelic Acid	473
CHAPTER XXXIII.—NAPHTHALENE AND ITS DERIVATIVES	474
Naphthalene	475
Naphthalene Tetrachloride—Nitro-Derivatives—Amino-Deriva- tives—Naphthols—Sulphonic Acids— α -Naphthaquinone— β -Naphthaquinone	481
The Orientation of Naphthalene Derivatives	488
Aromatic-Aliphatic Cyclic Compounds	489
Hydrindene, Indene, Hydrindone, Acenaphthene	490
CHAPTER XXXIV.—ANTHRACENE AND PHENANTHRENE	492
Anthracene	492
Anthraquinone—Alizarin—Phenanthrene—Phenanthraquinone —Diphenic Acid	496
CHAPTER XXXV.—PYRIDINE, QUINOLINE, ISOQUINOLINE AND OTHER HETEROCYCLIC COMPOUNDS	504

Contents.

v

	PAGE
Pyridine and its Derivatives	505
Piperidine	509
Derivatives of Pyridine—Pyridinecarboxylic Acids	510
Quinoline	513
Isoquinoline.	517
Furan, Thiophene, and Pyrrole	518
Reduction Products of Pyrrole	521
Indole and its Derivatives	524
CHAPTER XXXVI.—VEGETABLE ALKALOIDS	526
Alkaloids derived from Pyridine	529
Coniine—Nicotine—Piperine—Atropine—Cocaine	529
Synthetic Alkaloids	536
Eucaine—Novocaine—Stovaine	536
Alkaloids derived from Quinoline	537
Quinine—Cinchonine—Strychnine—Brucine	537
Alkaloids contained in Opium—Morphine, &c.	541
CHAPTER XXXVII.—AMINO-ACIDS AND RELATED COMPOUNDS	542
Amino-Acids—Resolution of <i>DL</i> -Amino-Acids—Ptomaines or Toxines	542
Polypeptides	546
Classification of Amino-Acids	547
Amino-Mono-Carboxylic Acids	548
Di-Amino-Mono-Carboxylic Acids	550
Mono-Amino-Di-Carboxylic Acids	550
Aromatic Amino-Acids	551
Heterocyclic Amino-Acids	551
Alkylamino-Acids and Related Compounds	552
CHAPTER XXXVIII.—URIC ACID AND OTHER PURINE DERIV- ATIVES	554
Uric Acid—Oxalylurea—Mesoxalylurea—Malonylurea	554
Syntheses of Uric Acid	557
The Purine Derivatives	559
Purine, Hypoxanthine, Xanthine, Theobromine, Caffeine, Adenine, Guanine	560
Guanidine	562
CHAPTER XXXIX.—SOME IMPORTANT COMPONENTS OF ANIMALS AND PLANTS	563
Lecithin, Glycocholic Acid, Taurocholic Acid, Cholic Acid, Cholesterol, Ergosterol, Calciferol	563

	PAGE
Hormones— <i>l</i> -Adrenaline, <i>l</i> -Thyroxine, Insulin	566
Vitamins	570
The Proteins	572
Hæmoglobin—Oxyhæmoglobin—Caseinogen	575
Chlorophyll—Gelatin	577
CHAPTER XL.—DYES AND THEIR APPLICATION	578
Derivatives of Triphenylmethane	584
Malachite Green, Pararosaniline, Rosaniline, Methyl Violet, Crystal Violet, Aniline Blue	585
The Phthaleins—Phenolphthalein	590
Xanthone Derivatives	591
Xanthone—Fluorescein—Eosin—Rhodamines	592
Derivatives of Anthracene	594
Alizarin Bordeaux R, Alizarin Cyanines, Indanthrene Blue R	594
Acridine Derivatives	596
Acridine—Acridone	596
Benzoflavin, Acridine Yellow R, Acridine Orange R	596
Azo-Dyes	597
Chrysoidine, Bismarck Brown, Helianthin, Resorcin Yellow, Paranitroaniline Red, &c.	600
Congo Red	603
Various Colouring Matters—Naphthol Yellow, Mauveine, Aniline Black, Methylene Blue, Primuline, Indigo, Phthalocyanines	604
NOTE ON THE IDENTIFICATION OF ORGANIC COMPOUNDS	609
LIST OF PREPARATIONS AND INDEX	follow 614

ORGANIC CHEMISTRY.

PART II.

CHAPTER XX.

PRODUCTION, PURIFICATION, AND PROPERTIES OF BENZENE.

Destructive Distillation of Coal.—When coal is strongly heated, out of contact with the air, it undergoes very complex changes, and yields a great variety of gaseous, liquid, and solid, volatile products, together with a non-volatile residue of coke. This process of dry, or destructive, distillation is carried out on the large scale in the manufacture of **coal-gas**, for which purpose the coal is heated in fire-clay or iron retorts, provided with air-tight doors; the gas and other volatile products escape from the retorts through pipes, and when distillation is at an end, the **coke**, a porous mass of impure carbon, containing the ash or mineral matter of the coal, is withdrawn.

The hot coal-gas passes first through a series of pipes or *condensers*, kept cool by immersion in water, or simply by exposure to the air, and, as its temperature falls, it deposits a considerable quantity of **tar** and **gas-liquor**, which are run together into a large tank; the gas is then passed through, and sprayed with, water, in *washers* and *scrubbers*, and, after having been further freed from tar, ammonia, carbon dioxide, and hydrogen sulphide, by suitable processes, it is led into the gas-holder and used for illuminating and heating purposes. The volume percentage composition of purified coal-gas is, very roughly: $H_2 = 47$, $CH_4 = 36$, $CO = 8$, $CO_2 = 2$, $N_2 = 3$, and hydrocarbons (acetylene, ethylene, benzene, &c.), other than methane, = 4, but varies *widely* with the nature of the coal and the temperature of the retorts.

The coal-tar and the gas-liquor in the tank separate into two layers; the upper one consists of gas-liquor or ammoniacal-

liquor (a yellow, unpleasant-smelling, aqueous solution of ammonium hydrogen carbonate, ammonium hydrosulphide, and numerous other compounds), from which some of the ammonia and ammonium salts of commerce are obtained. The lower layer in the tank is a dark, thick, oily liquid of sp. gr. 1.1 to 1.2, known as coal-tar. It is a mixture of a great number of organic compounds, and, although at one time it was considered to be an obnoxious by-product, it is now the sole source of very many substances of great industrial importance.

¹ More than 200 compounds have been proved to be present in coal-tar, but not all of these in any given sample; most of them are aromatic compounds (p. 352). Very large quantities of coal are also destructively distilled in coke-ovens, in the manufacture of coke for metallurgical operations; the products are similar to those obtained in a gas-works. The tar from the *low temperature carbonisation* of coal, for the production of a smokeless fuel (*coalite*), contains a much larger proportion of aliphatic substances (p. 351) than does ordinary coal-tar.

Fractional Distillation of Coal-tar.—In order to effect the separation of its components, the tar is submitted to fractional distillation; it is heated in large wrought-iron stills or retorts, the vapours which pass off are condensed in long iron or lead worms immersed in water, and the liquid distillate is collected in fractions. The point at which the receiver should be changed is ascertained by means of a thermometer, which dips into the tar, as well as by the character of the distillate. Sometimes this distillation is carried out under reduced pressure; there is then less decomposition of some of the valuable components of the tar.

In this way the tar is separated into the following fractions of which the given temperature limits are only approximate:

- I. Light oil or crude naphtha. Collected up to 170°.
- II. Middle oil or carbolic oil between 170° and 230°.
- III. Heavy oil or creosote oil 230° " 270°.
- IV. Anthracene oil above 270°.
- V. Pitch Residue in the still.

I. The first crude fraction separates into two layers—namely, gas-liquor (which the tar always retains mechanically to some extent) and an oil which is lighter than water, its sp. gr. being

¹ The consideration of those portions of the text printed in small type, except details of the preparation of typical compounds, may be postponed until the more important subject matter has been studied.

about 0.975, hence the name *light oil*. This oil is first redistilled from a smaller iron retort and the distillate is collected in three principal portions—namely, from 80–110°, 110–140°, and 140–170° respectively. All these fractions consist principally of **hydrocarbons**, but contain basic substances, such as **pyridine**, acidic substances, such as **phenol** or **carbolic acid**, and various other compounds; they are, therefore, separately agitated, first with caustic soda, which removes the phenols (p. 420), and then with sulphuric acid, which dissolves out the basic substances, and are washed with water after each treatment; afterwards they are again distilled. The oil, obtained in this way from the fraction collected between 80° and 110°, consists principally of the hydrocarbons, **benzene** and **toluene**, and is sold as ‘90 per cent. benzol’; that obtained from the fraction 110–140° consists essentially of the same two hydrocarbons (but in different proportions), together with **xylene**, and is sold as ‘50 per cent. benzol.’ These two products are not usually further treated by the tar-distiller, but are worked up in the manner described later. The oil from the fraction collected between 140° and 170° consists of the hydrocarbons, xylene, pseudocumene, mesitylene, &c., and is employed principally as ‘**solvent naphtha**,’ also as ‘burning naphtha.’

Commercial ‘90 per cent. benzol’ contains about 70 per cent., and ‘50 per cent. benzol,’ about 46 per cent. of pure benzene; the terms refer to the proportion of the mixture which passes over below 100° when the commercial product is distilled. Benzene, toluene, and xylene are known commercially as benzol, toluol, and xylol respectively.

II. The second crude fraction, or middle oil, collected between 170° and 230°, has a sp. gr. of about 1.02, and consists principally of **naphthalene** and **carbolic acid**. On being cooled, the naphthalene separates in crystals, which are drained and pressed to squeeze out liquid carbolic acid and other substances; the crude crystalline product is further purified by treatment with caustic soda and sulphuric acid successively, and is finally sublimed or distilled. The oil from which the crystals have been separated is agitated with warm caustic soda, which dissolves the carbolic acid and other phenols; the solution is then drawn off from the insoluble portions and treated with sulphuric acid, whereon crude carbolic acid separates as an oil, which is

washed with water and distilled ; it is thus separated into crystalline carbolic acid and a liquid mixture of phenols (cresylic acids), used in making Bakelite (p. 426), disinfectants (p. 429), &c.

III. The third crude fraction, collected between 230° and 270° , is a greenish-yellow, fluorescent oil, specifically heavier than water ; it contains **carbolic acid**, **cresol**, **naphthalene**, **anthracene**, and other substances, and is chiefly employed under the name of '**creosote oil**' for the preservation of timber.

IV. The fourth crude fraction, collected at 270° and upwards, consists of **anthracene**, **phenanthrene**, and other hydrocarbons, which are solid at ordinary temperatures, and which are deposited in crystals as the fraction cools ; after having been freed from oil by pressure, and further purified by digestion with solvent naphtha (which dissolves the other hydrocarbons more readily than it does the anthracene), the product is sold as '50 per cent. anthracene,' and is employed in the manufacture of various dyes. The oil drained from the anthracene is redistilled, to obtain a further quantity of the crystalline product, the non-crystallisable portions being known as '**anthracene oil**.'

V. The **pitch** in the still is run out while it is hot, and is employed for the preparation of varnishes, for the protection of wood and metal work, and for the production of asphalt.

A very large quantity of tar which has been freed from the more volatile components only, is used in road-making.

The table, opposite, summarises the results of tar distillation and shows the more important commercial products and a few of their uses ; most of the components of the tar, however, are employed principally in the manufacture of dye-stuffs.

The Isolation of Benzene.—The crude '90 per cent. benzol' of the tar-distiller consists essentially of a mixture of benzene and toluene, with small proportions of xylene and other substances ; on further fractional distillation it gives commercial benzene of high quality, which can be used for all ordinary purposes, but which still retains small quantities of toluene, paraffins, carbon disulphide, and other substances. For further purification, the benzene may be cooled in a freezing-mixture and the crystals quickly separated by filtration from the mother-liquor, which contains most of the impurities ; after this process has been repeated, the hydrocarbon should boil constantly at $80-81^{\circ}$.

COAL-TAR.

LIGHT OIL, up to 170°, redistilled			MIDDLE OIL, 170°-230°, separates into	HEAVY OIL, 230°-270°, used as creosote, and in Diesel engines.	ANTHRACENE OIL, above 270°, separates into	PITCH.
80-110°	110-140°	140-170°	residue	Crude naphthalene (crystals)	Crude anthracene (crystals)	
separately agitated with caustic soda and sulphuric acid consecutively, and again distilled		mixed with middle oil	Crystals pressed, treated with caustic soda and sulphuric acid successively, and sublimed, or distilled	Crude carbolic acid (liquid)	Anthracene oil (liquid) distilled	
90 per cent. benzol	50 per cent. benzol	Solvent naphtha	Naphthalene	Soluble portion treated with acid, and precipitated oil distilled	50 per cent. anthracene oil	
					Anthracene crystals (added to crude anthracene).	
				Crystalline carbolic acid		
				Liquid (impure) carbolic acid and cresols		
90 per cent. benzol	50 per cent. benzol	Solvent naphtha	Naphtha- Crystalline carbolic acid	Cresylic acids	50 per cent. Anthracene oil	Pitch. Brquettes. Varnishes. Roofing-felt. Road-making.
Motor fuel, Solvents, Dry Cleaning.			Fire-lighters.	Disinfectants.		

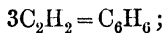
Even after having been submitted to crystallisation as well as distillation, the benzene is not pure, and when it is shaken with cold concentrated sulphuric acid, the latter darkens in colour owing to its having charred and dissolved the impurities; pure benzene, on the other hand, does not char with sulphuric acid, so that when the impure liquid is repeatedly shaken with small quantities of the acid, until the latter ceases to be discoloured, most of the foreign substances are removed.

Coal-tar benzene, which has not been purified in this way, contains a sulphur compound, C_4H_4S , named *thiophene*, which was discovered by V. Meyer (p. 520); the presence of thiophene is readily detected by shaking the sample with a little concentrated sulphuric acid and a trace of isatin (an oxidation product of indigo, p. 525), when the acid assumes a beautiful blue colour (indophenin reaction). Thiophene resembles benzene so closely in chemical and physical properties that it cannot be easily separated from the latter; it may, however, be extracted with sulphuric acid (above), which sulphonates and dissolves thiophene more readily than it does the hydrocarbon.

Although practically the whole of the benzene of commerce ('benzol') is prepared from coal-tar,¹ the hydrocarbon is also present in small proportions in wood-tar, in certain varieties of petroleum (p. 63), and in the tarry distillate of many other substances, such as shale, peat, &c.; it may, in fact, be produced, together with related compounds, by passing the vapour of alcohol, ether, petroleum, or of many other organic substances through a red-hot tube, under which conditions, no doubt, very complex changes occur.

Benzene, C_6H_6 , was discovered by Faraday in 1825 in the gas produced by the destructive distillation of vegetable oils and, twenty years later, was found in coal-tar by Hofmann.

It may be produced *synthetically* by merely heating acetylene at a dull-red heat,



many other hydrocarbons (toluene, diphenyl, indene, naphthalene, anthracene, phenanthrene, &c.) are formed at the same time.

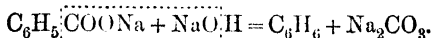
Acetylene, *free from air*, is collected over mercury in a piece of hard glass-tubing, closed at one end and bent at an angle of about 120° ; the tube is about half-filled with the gas, and a piece of copper gauze is wrapped round a portion of the horizontal limb, as shown (Fig. 24). This portion is then carefully heated with a Bunsen burner; after a short time

¹ Sometimes the coal-gas is washed (stripped) with some heavy oil, such as creosote, in order to extract from it benzene and other volatile hydrocarbons.

fumes appear, and minute drops of liquid condense on the colder parts of the tube. When it has been heated during about fifteen minutes, the tube is allowed to cool; the mercury then rises above its original level.

This conversion of acetylene into benzene is a process of polymerisation, and was first accomplished by Berthelot. It is a particularly important synthesis of benzene from its elements, because acetylene may be obtained by the direct combination of carbon and hydrogen or from calcium carbide (p. 89).

Benzene may also be obtained by heating benzoic acid (p. 451) or sodium benzoate with soda-lime, a reaction which recalls the formation of methane from sodium acetate,



All other benzene derivatives may be converted into the parent hydrocarbon by appropriate methods.

The analysis of benzene shows that it consists of 92·3 per cent. of carbon and 7·7 per cent. of hydrogen, a result which gives the empirical formula, CH ; since the vapour density of benzene is 39, its molecular weight is 78, which corresponds with the *molecular formula*, C_6H_6 .

At ordinary temperatures benzene is a colourless, highly refractive, mobile liquid of sp. gr. 0·8799 at 20°, which boils at 80·2°; when it is cooled in a freezing-mixture it solidifies to a crystalline mass, melting at 5·5°. It has a burning taste, a peculiar, not unpleasant smell, and is highly inflammable, burning with a luminous, very smoky flame, which is indicative of its richness in carbon; the luminosity of an ordinary coal-gas flame, in fact, is partly due to the presence of benzene. Although practically insoluble in water, benzene mixes with liquids such as ether and petroleum in all proportions; it readily dissolves fats, resins, iodine, and other substances which are insoluble in

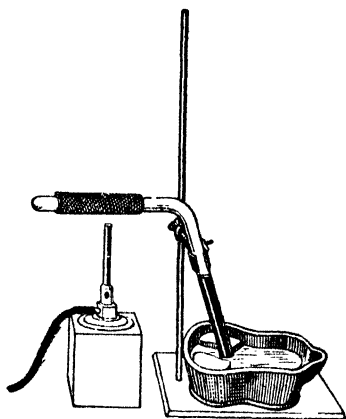
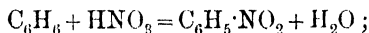


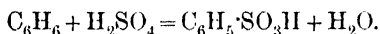
Fig. 24.

water, and for this reason is extensively used as a solvent and for cleaning purposes; it is also used as a motor-fuel, and for the manufacture of nitrobenzene (p. 383) and many other intermediates for the production of dyes, drugs, &c.

Benzene is a very stable compound, and, except when it is burned, is resolved into simpler substances only with great difficulty; when it is boiled with concentrated alkalis, for example, it undergoes no change, and even when it is heated with solutions of such vigorous oxidising agents as chromic acid or potassium permanganate, it is only very slowly attacked and decomposed, carbon dioxide, water, and traces of other substances being formed. Under certain conditions, however, benzene readily yields *substitution* products; concentrated nitric acid, even at ordinary temperatures, converts the hydrocarbon into *nitrobenzene* by the substitution of the univalent nitro-group, $-\text{NO}_2$, for an atom of hydrogen,



and concentrated sulphuric acid, slowly at ordinary, more rapidly at higher, temperatures, transforms it into *benzenesulphonic acid*,



Chlorine and bromine, in the absence of direct sunlight and at ordinary temperatures, react with benzene only very slowly, yielding *substitution* products, such as *chlorobenzene*, $\text{C}_6\text{H}_5\text{Cl}$, *bromobenzene*, $\text{C}_6\text{H}_5\text{Br}$, *dichlorobenzene*, $\text{C}_6\text{H}_4\text{Cl}_2$, &c.; when, however, some halogen carrier (p. 371), such as iron or iodine, is present, action takes place readily at ordinary temperatures, even in the dark, substitution products again being formed.

In bright sunlight the hydrocarbon is rapidly converted into *additive* products, such as *benzene hexachloride*, $\text{C}_6\text{H}_6\text{Cl}_6$, and *benzene hexabromide*, $\text{C}_6\text{H}_6\text{Br}_6$, by direct combination with six (but not more than six) atoms of the halogen.

It also combines with (molecular) hydrogen in the presence of catalysts, giving *hexahydrobenzene*, C_6H_{12} (p. 356).

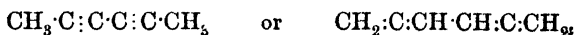
CHAPTER XXI.

CONSTITUTION OF BENZENE, AND ISOMERISM OF BENZENE DERIVATIVES.

It will be seen from the facts just stated that although benzene, like the paraffins, is an extremely stable substance, it differs from these hydrocarbons very considerably in chemical behaviour, more especially in being comparatively readily acted on by nitric acid and by sulphuric acid; further, when its properties are compared with those of the unsaturated hydrocarbons of the olefine or acetylene series, the contrast is even more striking, because the proportion of carbon to hydrogen in the molecule of benzene, C_6H_6 , would seem to indicate a relation to these unsaturated hydrocarbons.

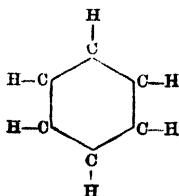
In order, then, to obtain some clue to the constitution of benzene, it is clearly of importance to consider carefully the properties of some unsaturated hydrocarbons of known constitution, and to ascertain in what respects they differ from those of benzene; for this purpose the compound *dipropargyl*, $CH:C\cdot CH_2\cdot CH_2\cdot C:CH$ (p. 95), may be chosen, as it has the same molecular formula as benzene.

Now, although dipropargyl and benzene are isomeric, they are completely different in chemical behaviour; the former is very unstable, readily undergoes polymerisation, combines energetically with bromine, giving *additive* compounds, and is immediately oxidised by various reagents; it shows, in fact, all the properties of an unsaturated hydrocarbon of the acetylene series. Benzene, on the other hand, is extremely stable, is comparatively slowly acted on by bromine, giving (usually) *substitution* products, and is oxidised only with difficulty even by the most vigorous reagents. Since, therefore, dipropargyl must be represented by the above formula in order to account for its method of formation and chemical properties, the constitution of benzene could not possibly be expressed by any similar formula, such as,



because compounds similar in constitution are always more or less similar in properties, and any such formula would not afford the slightest indication of the fundamental differences between benzene and ordinary unsaturated hydrocarbons of the olefine or acetylene series.

These and many other facts, which were established during the investigation of benzene and its derivatives, led Kekulé (1865) to conclude that *the six carbon atoms in benzene form a closed-chain or nucleus, that the molecule of benzene is symmetrical, and that each carbon atom is directly united with one (and only one) atom of hydrogen*, as represented below :

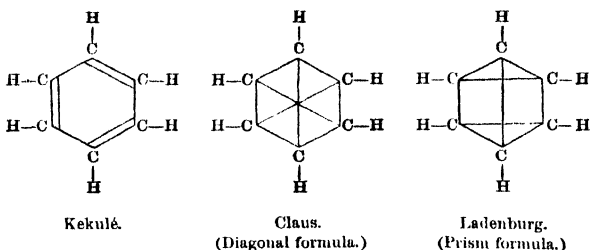


These views are now universally accepted, and the evidence on which they are based is given later ; there is, however, at least one important point which has still to be discussed—namely, what is the best way of representing the state of combination of the carbon atoms ?

The structural formulæ of organic compounds are based on the assumption that carbon is always quadrivalent¹; this assumption, as already explained (p. 45), is expressed in graphic formulæ by drawing four lines from the symbol of each carbon atom, in such a way as to show with which other atoms or groups the particular carbon atom in question is directly united. Now, in the case of benzene, it is clear that two of the four lines or bonds, which represent the valencies of each carbon atom, must be drawn to meet two other carbon symbols, because unless each carbon atom is directly united with two others, the six could not together form a closed-chain ; a third line or bond must be drawn to meet a hydrogen symbol, because each carbon atom is directly united with hydrogen. In this way, however, only three of the four units of valency of each carbon atom are shown, and the question

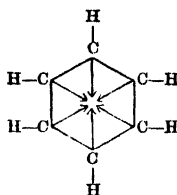
¹ In a relatively insignificant number of compounds carbon acts as a trivalent element, but such substances are unsaturated and usually unstable.

remains, how may the fourth one be represented so as to give the clearest indication of the behaviour of benzene? Many chemists have attempted to answer this question, and several constitutional formulæ for benzene have been put forward; that suggested by Kekulé in 1865 was for a long time considered to be the most satisfactory, but others, such as those of Claus and Ladenburg, also received support:



It will be seen that all these three formulæ portray the molecule of benzene as a symmetrical closed-chain of six carbon atoms, and that they differ, in fact, only as regards the representation of the way in which the carbon atoms are united with one another; this difference, moreover, only concerns the state or condition of one of the units of valency of each carbon atom. In Kekulé's formula, for example, two lines (or a double bond) are drawn between alternate carbon atoms, a method of expression which is the same as that adopted in the case of ethylene and other olefines; in the formulæ of Claus and Ladenburg, on the other hand, each carbon atom is represented as being directly united with three others (but with a different three in the two cases).

As it is unnecessary to enter here into a full discussion of the relative merits of the above three formulæ, it may be stated briefly that those of Claus and Ladenburg do not accord with certain facts which have been established by Baeyer and others, while that of Kekulé suggests a close relationship between benzene and the olefines, which does not exist. In order to meet these objections, it was proposed by Armstrong, and shortly afterwards by Baeyer, that the constitution of benzene should be represented by the formula,



Armstrong-Baeyer (Centric formula).

One unit of valency of each of the (six) carbon atoms is here represented as being *directed* towards a centre (as shown by the arrows) in order to denote that this particular unit does not form a link with a single atom only, in the usual way, but has a general attraction for all the other carbon atoms of the nucleus. This symbol, named by Baeyer the *centric formula*, was preferred to Kekulé's formula, because it did not represent the molecule as containing 'double bindings' similar to those shown in the formulæ of the olefines, and so did not imply that benzene and the olefines are similar in chemical behaviour.

The centric formula, however, is not entirely satisfactory; when a model of it is examined, it will be seen that the hydrogen atoms do not lie in the same plane as the carbon atoms, whereas it is known from X-ray examination (p. 44) and other evidence that they actually do so, in accordance with the Kekulé structure.

The further discussion of this problem, in the light of considerations based on the electronic theory of valency (Part III.), has led to the conclusion that *one of the four units of valency of each carbon atom is not concerned with one other carbon atom only, but is distributed over the molecule*; as this particular bond cannot be represented in the ordinary way, the constitution of benzene is expressed by the symbol on p. 334.

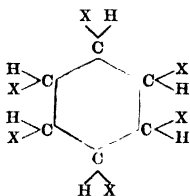
This symbol (or formula), although incomplete, summarises the main facts concerning the structure of the hydrocarbon, and also serves to elucidate the general behaviour of benzene and the isomerism of its derivatives as shown below.

In the first place, it may be repeated that benzene is a very stable substance; although it is acted on by powerful reagents, such as nitric acid, sulphuric acid, chlorine, and bromine, and thereby converted into new compounds, all these products or derivatives of benzene contain *six* carbon atoms; the hydrogen atoms

may be displaced by certain atoms or groups, which in their turn may be displaced by others; but, in spite of all these changes, the six atoms of carbon remain, forming, as it were, a stable and permanent **nucleus**. This is expressed in the formula by the closed-chain of six carbon atoms, all of which are represented in the same state of combination, which implies that there is no reason why one should be attacked and taken away more readily than another.

Again, a great many compounds, which are known to be derivatives of benzene, contain more than six atoms of carbon; when, however, such compounds are treated in a suitable manner, they are easily converted into substances containing six, but not *less* than six, atoms of carbon. This fact shows that in these benzene derivatives there are six atoms of carbon which are in a different state of combination from the others, and thus emphasises the existence of the stable nucleus; the additional carbon atoms, not forming part of this nucleus, are more easily attacked and removed.

Further, it must be remembered that although benzene usually gives substitution products, it is capable, under certain conditions, of forming additive products (p. 332); this behaviour is also accounted for. In the formula, only three of the four units of valency of each carbon atom are shown to be normally engaged; each carbon atom, therefore, is capable of combining directly with one univalent atom or group, so as to form finally a fully saturated compound of the type,



Isomerism of Benzene Derivatives.

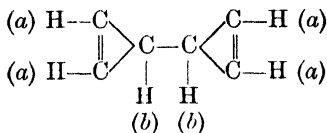
The most convincing evidence that the molecule of benzene is *symmetrical* is derived from a study of the isomerism of benzene derivatives. It has been proved, in the first place, that it is possible to substitute 1, 2, 3, 4, 5, or 6 univalent atoms or groups for a corresponding number of the hydrogen atoms in benzene, compounds such as *bromobenzene*, C_6H_5Br , *dinitrobenzene*, $C_6H_4(NO_2)_2$, *trimethylbenzene*, $C_6H_3(CH_3)_3$, *tetrachlorobenzene*, $C_6H_2Cl_4$, *penta-methylbenzene*, $C_6H(CH_3)_5$, and *hexacarboxybenzene*, $C_6(COOH)_6$,

being produced ; the substituting atoms or groups, moreover, may be identical or different.

The examination of such substitution products of benzene has shown that when only *one* atom of hydrogen is displaced by any given atom or group, the same compound is always produced—that is to say, the *mono-substitution products of benzene exist in one form only* ; when, for example, *nitrobenzene*, $C_6H_5 \cdot NO_2$, is prepared, no matter in what way this change may be brought about, the same substance is always produced.

This might be explained, of course, by the assumption that one particular hydrogen atom was always displaced by the nitro-group ; when, for example, acetic acid is treated with sodium hydroxide, since only one of the four hydrogen atoms is displaceable, the same salt is invariably produced. In the case of benzene, however, it has been shown that although every one of the six hydrogen atoms may be displaced in turn, the same substance is always formed.

The only possible conclusion to be drawn from this fact is that *all* the hydrogen atoms are in exactly similar positions relatively to the rest of the molecule ; if this were not so, and the constitution of benzene were represented by any formula such as the following,

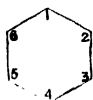


in which some of the hydrogen atoms (*a*) are differently situated from the others (*b*), it would be possible to obtain isomeric mono-substitution products.

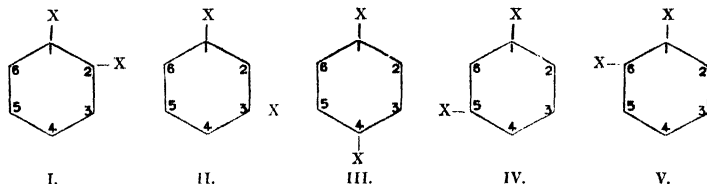
By the substitution of *two* univalent atoms or groups for two of the atoms of hydrogen in benzene, *three*, but not more than three, isomerides are obtained ; there are, for example, three *dinitrobenzenes*, $C_6H_4(NO_2)_2$, three *dibromobenzenes*, $C_6H_4Br_2$, three *dihydroxybenzenes*, $C_6H_4(OH)_2$, three *nitrohydroxybenzenes*, $C_6H_4(NO_2) \cdot OH$, and so on.

Now the existence of the three isomerides can be easily accounted for with the aid of the closed-chain structure given on

p. 334, which, for this purpose, may conveniently be represented by a hexagon, numbered as shown, the symbols C and H and the lines which are there drawn between them being omitted, for the sake of simplicity :



Suppose that any mono-substitution product, C_6H_5X , which, as already stated, exists in one form only, is converted into a di-substitution product, $C_6H_4X_2$; then if the position occupied by the atom or group (X), which is first introduced, is numbered 1, the second atom or group may have substituted any one of the hydrogen atoms at 2, 3, 4, 5, or 6, giving a substance the constitution of which might be represented by one of the following five formulæ¹:



These five formulæ, however, represent *three* isomeric substances, and three only. The formula iv. represents a compound in which the several atoms occupy the same relative positions as in the substance represented by II., and for the same reason the formula v. is identical with I. Although there is at first sight an apparent difference, a little consideration will show that this is simply due to the fact that the formulæ are viewed from one point only; if the formulæ iv. and v. are written on thin paper and then viewed *through* the paper, it will be seen that they are identical with II. and I. respectively. Each of the formulæ I., II., and III., however, represents a different substance, because in no two cases are all the atoms in the same relative positions; in other words, such di-substitution products of benzene exist in three isomeric forms.

¹ Strictly speaking, these are merely symbols, but are usually called formulæ because they serve as substitutes for the more complete structural representations (compare p. 336).

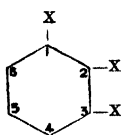
In the foregoing examples the two substituent atoms or groups have been considered to be identical ; but even when they are different, experience has shown that only three di-substitution products can be obtained, and this fact, again, is explained by the accepted formula. When in the above five symbols a Y is written in the place of one X, to express a difference in the substituent groups, it will be seen that, as before, the formula i. is identical with v., and ii. with iv., but that i., ii., and iii. all represent different arrangements of the atoms—that is to say, three different substances.

Since the di-substitution products of benzene exist in three isomeric forms, it is necessary to have some way of distinguishing them by name ; for this reason all di-substitution products, which are found to have the constitution represented by the formula i., are called **ortho**-compounds, and the substituent atoms or groups are said to be in the ortho- or 1:2-position to one another ; those substances, which may be represented by the formula ii., are termed **meta**-compounds, and the substituent atoms or groups are spoken of as occupying the meta- or 1:3-position ; the term, **para**, is applied to compounds represented by the formula iii., in which the atoms or groups are situated in the para- or 1:4-position.

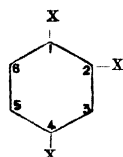
Ortho-compounds, then, are those in which it is concluded, for reasons given later (p. 343), that the two substituent atoms or groups are combined with carbon atoms, which are themselves *directly united*. Instead of the constitution of any ortho-compound being expressed by the formula i., which represents the substituent atoms or groups as combined with the carbon atoms 1 and 2, the result would be just the same if the substituents were shown to be united with the carbon atoms 2 and 3, 3 and 4, 4 and 5, 5 and 6, or 6 and 1 ; all such arrangements would be identical because the benzene molecule is symmetrical, and the numbering of the carbon atoms simply a matter of convenience. In a similar manner the substituent atoms or groups in meta-compounds may be represented as combined with any two carbon atoms which are not themselves directly united, but linked together by one carbon atom ; it is quite immaterial which two carbon atoms are chosen, since atoms or groups occupying the 1:3-, 2:4-, 3:5-, 4:6-, or 5:1-position are identical as regards their

relation to all the other atoms of the molecule. For the same reason para-compounds may be represented by placing the substituent atoms or groups in the 1:4-, 2:5-, or 3:6-position.

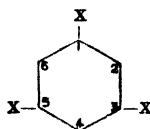
When more than two atoms of hydrogen in benzene are displaced, it has been found that the number of isomerides varies according as the substituent atoms or groups are identical or not. By displacing *three* atoms of hydrogen by three *identical* atoms or groups, *three* isomerides can be obtained, three *trimethylbenzenes*, $C_6H_3(CH_3)_3$, for example, being known. Again, the existence of these isomerides can be easily accounted for, since their constitutions may be represented as follows:



1:2:3- or Adjacent.



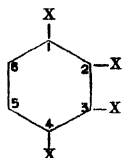
1:2:4- or Unsymmetrical.



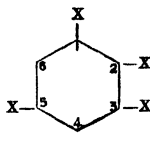
1:3:5- or Symmetrical.

No matter in what other positions the substituent atoms or groups are placed, it will be found that the arrangement is the same as that represented by one of these three formulæ; the position 1:2:3, for example, is identical with 2:3:4, 3:4:5, &c.; 1:3:4 with 2:4:5, 3:5:6, &c.; and 1:3:5 with 2:4:6. For the purpose of distinguishing such tri-substitution products by names, the terms given above are often employed.

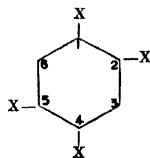
The tetra-substitution products of benzene, in which all the substituent atoms or groups are identical, also exist in three isomeric forms represented by the following formulæ:



1:2:3:4.



1:2:3:5.



1:2:4:5.

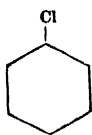
When, however, five or six atoms of hydrogen are displaced by identical atoms or groups, only one substance is produced.

When more than two atoms of hydrogen are displaced by atoms or groups which are not all identical, the number of isomerides which can be obtained is very considerable. In the case of any tri-substitution product, $C_6H_3X_2Y$, for example, six isomerides might be formed, as

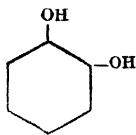
may be easily seen by assigning a definite position, say 1, to Y; the isomerides would then be represented by formulæ in which the groups occupied the positions 1:2:3, 1:2:4, 1:2:5, 1:2:6, 1:3:4, or 1:3:5, all of which would be different (compare p. 347). In a similar manner the number of isomerides theoretically obtainable in the case of all benzene derivatives, however complex, may be deduced with the aid of the hexagon symbol.

All the cases of isomerism considered up to the present have been due to the different relative positions of the substituent atoms or groups combined with the benzene nucleus; as, however, many benzene derivatives contain groups of atoms, which themselves exhibit isomerism, such groups may give rise to isomerides comparable with those of the paraffins, alcohols, &c. There are, for example, two isomeric hydrocarbons of the composition, $C_6H_5 \cdot C_3H_7$, namely, *propylbenzene*, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$, and *isopropylbenzene*, $C_6H_5 \cdot CH(CH_3)_2$, just as there are two isomeric compounds of the composition, C_3H_7I . As, moreover, propyl- and isopropyl-benzene, $C_6H_5 \cdot C_3H_7$, are isomeric with the three (ortho-, meta-, and para-) *ethylmethylbenzenes*, $C_6H_4(C_2H_5) \cdot CH_3$, and also with the three (adjacent, symmetrical, and unsymmetrical) *trimethylbenzenes*, $C_6H_3(CH_3)_3$, there are in all eight hydrocarbons of the molecular formula, C_9H_{12} , derived from benzene.

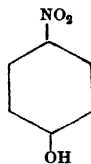
In studying the isomerism of benzene derivatives, the clearest impressions will be gained by making use of a simple, unnumbered hexagon to represent C_6H_6 , and by expressing the constitutions of simple substitution products by formulæ (or symbols, footnote p. 339) such as,



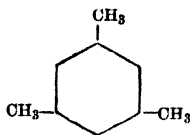
Chlorobenzene.



Catechol.



Nitrophenol.



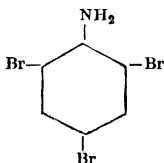
Trimethylbenzene.

The omission of the symbols C and H is attended by little, if any, disadvantage, because, in order to convert the above into the ordinary molecular formulæ, it is only necessary to write C_6 instead of the hexagon, and then to count the unoccupied corners of the hexagon to find the number of hydrogen atoms of the nucleus, the substituent atoms or groups being added afterwards.

In the case of *chlorobenzene*, for example, there are five unoccupied corners, so that the molecular formula is C_6H_5Cl ; whereas in the case of *trimethylbenzene* there are three, and the formula, therefore, is $C_6H_3(CH_3)_3$.

As, however, such graphic expressions occupy a great deal of space, their constant use in a text-book is inconvenient, and other methods are adopted. The most usual course in the case of the di-derivatives is to employ the terms *ortho*-, *meta*-, and *para*-, or simply the letters **o**, **m**, and **p**, as, for example, *ortho-dinitrobenzene* or **o**-*dinitrobenzene*, *meta-nitroaniline* or **m**-*nitroaniline*, *para-nitrophenol* or **p**-*nitrophenol*. The relative positions of the atoms or groups may also be expressed by numbers; **o**-*chloronitrobenzene*, for example, may be described as 1:2-*chloronitrobenzene*, as $C_6H_4 \begin{smallmatrix} \text{Cl} & (1) \\ \text{NO}_2 & (2) \end{smallmatrix}$, or as $C_6H_4 \text{Cl}^1 \text{NO}_2^2$, the corresponding *para*-compound as 1:4-*chloronitrobenzene*, as $C_6H_4 \begin{smallmatrix} \text{Cl} & (1) \\ \text{NO}_2 & (4) \end{smallmatrix}$, or as $C_6H_4 \text{Cl}^1 \text{NO}_2^4$, and so on.

In the case of the tri-derivatives the terms *symmetrical*, *unsymmetrical*, and *adjacent* (compare p. 341) may be employed when all the atoms or groups are the same, but when they are different the constitution of the compound is expressed with the aid of numbers; the *tribromoaniline* of the constitution,



for example, is represented by $C_6H_2Br_3 \cdot NH_2$ [$NH_2 : Br : Br : Br$], or by $C_6H_2Br_3 \cdot NH_2$ [$NH_2 : 3Br = 1:2:4:6$], but it is of course quite immaterial from which corner of the hexagon the numbering is commenced.

The Orientation of Benzene Derivatives.

Since the di-substitution products of benzene, such as *dibromobenzene*, $C_6H_4Br_2$, *dihydroxybenzene*, $C_6H_4(OH)_2$, and *nitroaniline*, $C_6H_4(NO_2) \cdot NH_2$, exist in three isomeric forms, it is now necessary to consider how the constitution of any such derivative is established; that is to say, how to ascertain whether the substituents

are arranged or *orientated* in the ortho-, meta-, or para-position in the molecule of the compound.

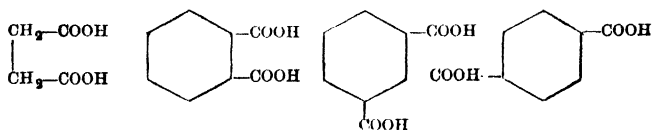
Now the methods which are adopted in the *orientation* of di-substitution products at the present time are comparatively simple, but they are based on the results of work which has extended over many years. One of the more important results of such work has been to prove that a given di-substitution product of benzene may be converted by more or less direct methods into many of the other di-substitution products of the *same type*. *Ortho-dinitrobenzene*, $C_6H_4(NO_2)_2$, for example, may be transformed into *o-diaminobenzene*, $C_6H_4(NH_2)_2$, *o-dihydroxybenzene*, $C_6H_4(OH)_2$, *o-dibromobenzene*, $C_6H_4Br_2$, *o-dimethylbenzene*, $C_6H_4(CH_3)_2$, and so on; corresponding changes are also possible with meta- and para-compounds. If, therefore, it can be found to which type a given di-substitution product belongs, the orientations of other di-substitution products, which may be derived from, or converted into, this compound, are thereby determined. There are, for example, three *dinitrobenzenes*, melting at 90° , 118° , and 173° respectively; now if it could be proved that the compound melting at 90° is a meta-derivative, then it might be concluded that the diamino-, dihydroxy-, dibromo-, and other di-derivatives of benzene, obtained from this particular dinitro-compound by substituting other atoms or groups for the two nitro-groups, must also be meta-compounds; it would also be known that the di-derivatives of benzene obtained from the other two dinitrobenzenes, melting at 118° and 173° respectively, in a similar manner, are either ortho- or para-compounds as the case may be.

In a few reactions, particularly in those which take place at a high temperature, the initial product may undergo a subsequent change; an ortho- or para-compound, for example, may be transformed into a meta-derivative (compare p. 423).

Obviously, then, it is necessary, in the first place, to orientate or determine the constitutions of those di-derivatives, which are afterwards to be used as standards.

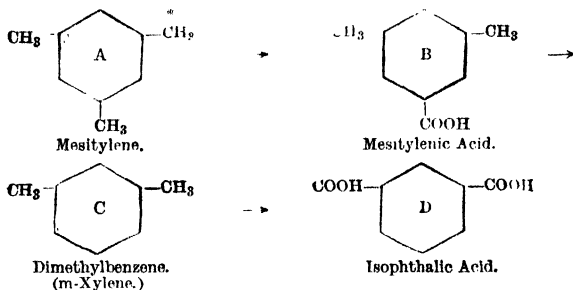
As an illustration of the methods and arguments originally employed in the solution of problems of this nature, the cases of the dicarboxy- and dimethyl-derivatives of benzene may be considered. Of the three benzenedicarboxylic acids, $C_6H_4(COOH)_2$, one—namely, *phthalic acid* (p. 457)—is very readily converted

into its anhydride, but all attempts to prepare the anhydrides of the other two acids (*isophthalic acid* and *terephthalic acid*, p. 459) have been unsuccessful. It is assumed, therefore, that the acid which gives the anhydride is the *o*-compound, because, from a study of the behaviour of many other dicarboxylic acids, it has been found that anhydride formation takes place most readily when the two carboxyl-groups are severally combined with two carbon atoms, which are themselves directly united, as, for example, in the case of succinic acid. In other words, if the graphic formulæ of succinic acid and of the three isomeric benzenedicarboxylic acids are compared, it will be evident that the relative positions of the two carboxyl-groups in the *o*-compound seem to be the same as in succinic acid, but this is quite otherwise in the case of the *m*- and *p*-compounds:



For this reason, phthalic acid may be provisionally regarded as an *ortho*-benzenedicarboxylic acid.

Again, the hydrocarbon, *mesitylene*, one of the three *trimethylbenzenes*, may be produced synthetically from acetone (p. 353), and its formation in this way can be explained in a simple manner, only on the assumption that mesitylene is the *symmetrical* trimethylbenzene of the constitution, (A):



When this hydrocarbon is carefully oxidised, it yields an acid, (B), of the composition, $C_6H_3(CH_3)_2 \cdot COOH$ (by the conversion of one of the methyl-groups into carboxyl), from which a *di*-

methylbenzene, $C_6H_4(CH_3)_2$, (C), is easily obtained by heating the acid with soda-lime. This dimethylbenzene, therefore, is a *meta*-compound, because no matter which of the original three methyl-groups in mesitylene has been finally displaced by hydrogen, the remaining two must occupy the *m*-position. Now when this *m*-dimethylbenzene is oxidised with chromic acid, it is converted into a dicarboxylic acid, (D)—namely, *isophthalic acid*, $C_6H_4(COOH)_2$ —which, therefore, must also be regarded as a *meta* compound. The constitutions of two of the three isomeric dicarboxy-derivatives of benzene having been thus determined, that of the third—namely, *terephthalic acid*, the *para*-compound—is also settled.

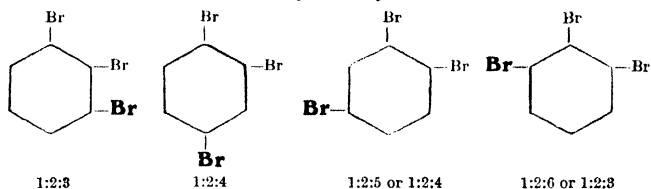
The three dicarboxylic acids having been orientated, it is a comparatively simple matter to determine the structures of the three dimethylbenzenes; one of them having been found to be the *meta*-compound, all that is necessary is to submit each of the other two to oxidation, and that which gives phthalic acid will be the *ortho*-compound, whilst that which yields terephthalic acid will be the *para*-derivative. Moreover, the orientation of any other di-substitution product of benzene may now be accomplished, provided that it is possible to convert this product into one of these standards by simple substitutions. If, for example, directly, or indirectly, the following substitutions could be carried out,

$C_6H_4(NO_2)_2 \rightarrow C_6H_4(NH_2)_2 \rightarrow C_6H_4(OH)_2 \rightarrow C_6H_4Br_2 \rightarrow C_6H_4(CH_3)_2$,
and the final product is proved to be *para*-dimethylbenzene, *all* the compounds concerned must also be classed as *para*-derivatives of benzene, unless there is convincing evidence to the contrary.

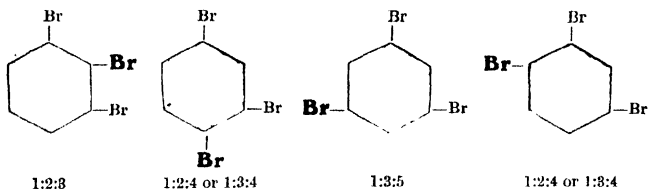
As the methods which have just been indicated are based principally on arguments drawn from analogy, or deductions as to the probable course of a given reaction, the conclusions to which they lead cannot be accepted without reserve; there are, however, other ways in which it is possible to distinguish between *ortho*-, *meta*-, and *para*-compounds, without making any assumptions, and, of these, that employed by Körner in 1874 is the most important.

Körner's method for the orientation of a di-substitution product of benzene is based on the fact that when any benzene derivative, $C_6H_4X_2$, is converted into a tri-derivative by the further displace-

ment of hydrogen of the nucleus, the number of isomerides which may be obtained from an *ortho*-, *meta*-, or *para*-compound is different in all three cases; if, therefore, the number of these products can be ascertained, the constitution of the original di-derivative is established. In the investigation of the *dibromobenzenes*, $C_6H_4Br_2$, for example, three isomerides, melting at 7.8° , -6.5° , and 89° respectively, were discovered, and the question arose, which of these is the *ortho*-, which the *meta*-, and which the *para*-compound? Suppose now that each of these isomerides is separately converted into a *tribromobenzene*, $C_6H_3Br_2Br$; then, if it is the *ortho*-dibromo-compound, it is possible to obtain from it *two*, but only two, tribromobenzenes, because, although there are four hydrogen atoms, any one of which may be displaced, the third formula shown below is identical with the second, and the fourth with the first, the relative positions of all the atoms being the same in the two cases respectively ¹:

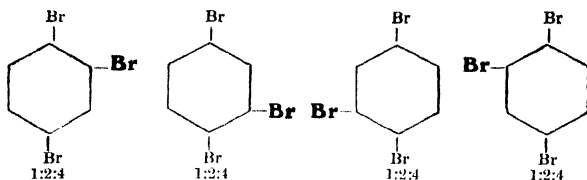


If, on the other hand, the dibromobenzene is the *meta*-compound, it might yield *three*, but only three, isomeric tri-derivatives, which would be represented by the first three of the following formulæ, the fourth being identical with the second:



Finally, if the substance in question is *para*-dibromobenzene, it could give *one* tri-derivative only, the following four formulæ being identical, and representing the 1:2:4 derivative:

¹ It is of course immaterial from which corner of the hexagon the numbering starts.



Experiments showed that the compound melting at 7.8° gave *two* tribromobenzenes (m.p. 44° and 87° respectively), it is, therefore, the *ortho*-compound. The dibromobenzene melting at -6.5° gave *three* such derivatives (m.p. 44° , 87° , and 119° respectively), and is thus proved to be the *meta*-compound; the isomeride melting at 89° gave only *one* (m.p. 44°), and, therefore, is the *para*-compound. Obviously this method may be applied in the case of *any* di-substitution product, $C_6H_4X_2$, provided that the derivatives, $C_6H_3X_2Y$ (Y may or may not be identical with X), can be separated and identified.

At the present time, the orientation of any new di-derivative of benzene is usually an easy task, because the new substance may be converted into one or other of the many compounds of known constitution by simple substitutions.

The main facts relating to the structure of benzene may now be summarised as follows:

(1) Benzene behaves towards nitric and sulphuric acids and (usually) towards halogens as a saturated compound, and not as if it had a structure similar to that of dipropargyl or other unsaturated hydrocarbon.

(2) Benzene is very stable and all its derivatives, containing more than six carbon atoms, can be converted by suitable means into substances containing only six carbon atoms. These six atoms, therefore, form a stable core or nucleus.

(3) It can be proved that all the six hydrogen atoms in benzene are identically situated.

(4) The study of the isomerism of its substitution products forms the final proof that the molecule of benzene consists of a symmetrical closed-chain of six carbon atoms, each of which is combined with an atom of hydrogen.

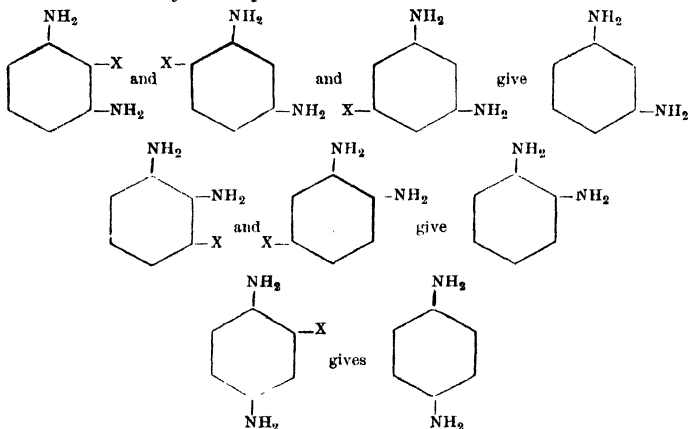
From the account of Körner's method given above it will be seen that one of the three isomeric tribromobenzenes (m.p. 44°) is obtained from the *ortho*-, the *meta*- and the *para*-di-derivative; this particular com-

pound must be the 1:2:4-tribromo-derivative, which therefore has itself been orientated. The second compound (m.p. 87°) formed from *o*-dibromobenzene is therefore the 1:2:3-tri-derivative, which is identical with one of the compounds obtained from *m*-dibromobenzene; the remaining tribromobenzene (m.p. 119°), obtained together with the 1:2:3- and the 1:2:4-compounds from *m*-dibromobenzene must be the 1:3:5-tri-substitution product. These three compounds might then serve for the orientation of other tri-derivatives of benzene, $C_6H_3X_3$, which might be obtained from them by substitution.

Körner did not actually prepare the tri- from the di-bromo-derivatives directly; he first converted the latter separately into their nitro-substitution products, $C_6H_3Br_2 \cdot NO_2$, isolated the various isomerides formed from each, and then displaced the nitro-group by bromine by the usual methods. In this way, therefore, the orientation of the *six* isomeric nitrodibromobenzenes, and the *six* isomeric aminodibromobenzenes, obtained from them by reduction, was also accomplished.

Although simple in theory, the experimental difficulties of Körner's method are very considerable owing to the 'directing' influence (p. 382) of the substituents already present. Thus, although theoretically any meta-compound, for example, should yield three tri-derivatives, one or two of these may be formed in such small quantities, if at all, that the isolation and identification of one or both may be a very difficult task.

The converse of Körner's method was used by Griess, who distilled the *six* known diaminobenzoic acids with lime: the phenylenediamine obtained from three of these acids is clearly the meta-compound, that formed from two of the acids only is the *ortho*-base, and that obtained from one acid only is the *para*-derivative ($X = -COOH$):

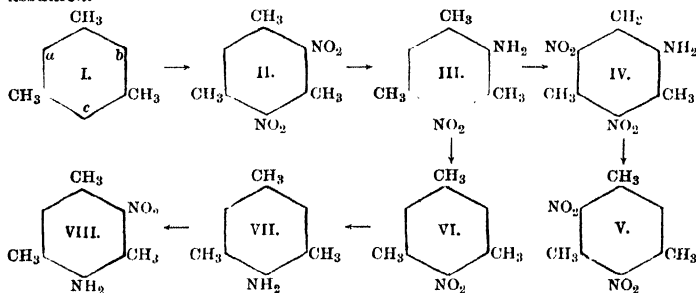


As a simple example of the way in which a tri-substitution derivative of benzene is usually orientated, the case of a hydroxyaminobenzoic acid,

$C_6H_3(OH)(NH_2)COOH$, may be taken. When the acid is distilled with lime, the carboxyl-group is displaced by hydrogen and *o*-hydroxyaniline is formed; the $HO-$ and the NH_2- groups are therefore in the ortho-position to one another. By the elimination of the NH_2- group of the acid, *p*-hydroxybenzoic acid is produced; the $HO-$ and the $COOH-$ groups are therefore para- to one another. The constitution of the hydroxyaminobenzoic acid is thus proved to be $OH:NH_2:COOH = 1:2:4$.

As an illustration of the manner in which it has been proved that at least three of the hydrogen atoms in benzene are identically situated, the case of mesitylene, investigated by Ladenburg, may be considered: Mesitylene, I., was converted into dinitromesitylene, II., which, when partially reduced gave a nitromesidine, III. This base (in the form of its acetyl-derivative, p. 393) nitrated, gave the compound, IV., from which, by the displacement of the amino-group there was obtained a dinitromesitylene, V.; this product was identical with II., and therefore the hydrogen atoms *a* and *b* occupy identical positions in the molecule of mesitylene.

Starting from III., the nitro-compound VI. was obtained by substituting an atom of hydrogen for the amino-group, and then by reduction the base VII. was prepared; this substance (as acetyl-derivative) gave on nitration a nitroaminomesitylene, VIII., which was identical with III.; the hydrogen atoms *b* and *c*, or *a* and *c* (because the nitro-group may have displaced the atom *a* or *b*) are therefore identically situated. But since $a=b$, $a=b=c$. It is also proved by these results that mesitylene must be 1:3:5-trimethylbenzene, as already assumed.



These results may also be summarised as follows :

	<i>a</i>	<i>b</i>	<i>c</i>		<i>a</i>	<i>b</i>	<i>c</i>
II.	H	NO ₂	NO ₂	→	VI.	H	NO ₂
III.	H	NH ₂	NO ₂		VII.	H	NH ₂
IV.	NO ₂	NH ₂	NO ₂			H	NO ₂
V.	NO ₂	H	NO ₂		VIII.	{	or
						NO ₂	H
							NH ₂

II. = V., ∴ $a=b$

VIII. = III., ∴ $c=a$ or b

∴ $a=b=c$.

Ladenburg also showed that four of the six hydrogen atoms in benzene are similarly situated. Phenol, $C_6H_5 \cdot OH$, or hydroxybenzene, with the aid of phosphorus pentabromide, may be directly converted into bromobenzene, C_6H_5Br , and the latter may be transformed into benzoic acid (or benzenecarboxylic acid), $C_6H_5 \cdot COOH$, with the aid of sodium and carbon dioxide; as these three substances are produced from one another by simple reactions, there is every reason to suppose that the carboxyl-group in benzoic acid is united with the same carbon atom as the bromine atom in bromobenzene and the hydroxyl-group in phenol; that is to say, that the same hydrogen atom (A) has been displaced in all three cases. Now three different hydroxybenzoic acids of the composition, $C_6H_4(OH) \cdot COOH$, are known, and these three compounds may be either converted into, or obtained from, benzoic acid, $C_6H_5 \cdot COOH$ (A), the difference between them being due to the fact that the hydroxyl group has displaced a different hydrogen atom (B, C, D) in each case. Each of these hydroxybenzoic acids forms a calcium salt which yields phenol when it is heated (the carboxyl-group being displaced by hydrogen), and the three specimens of phenol thus produced are identical with the original phenol; it is evident, therefore, that at least four (A, B, C, D) hydrogen atoms in benzene occupy the same relative positions in the molecule. By analogous methods it can be shown that this is true of all six hydrogen atoms.

CHAPTER XXII.

GENERAL PROPERTIES OF AROMATIC COMPOUNDS.

Classification of Organic Compounds.—The examples given in the foregoing pages will have afforded some indication of the large number of compounds, which it is possible to prepare from benzene, by the substitution of various elements or groups for atoms of hydrogen. As the substances formed in this way, and many other benzene derivatives, which occur in nature, are obtained from coal-tar, or may be prepared synthetically, retain to a greater or less extent the characteristic chemical behaviour of benzene, and differ in many respects from the paraffins, alcohols, acids, and all other compounds previously considered (Part I.), it is convenient to place benzene and its derivatives in a separate group.

Organic compounds, therefore, are classed in two principal divisions, the **fatty** or **aliphatic** (from *ἄλειφαρ*, fat) and the

aromatic. The word 'fatty,' originally applied to some of the higher acids of the $C_nH_{2n}O_2$ series (p. 146), is now used to denote all compounds which may be considered as derivatives of methane; all the compounds described in Part I. belong to the fatty or aliphatic division. Benzene and its derivatives, on the other hand, are classed in the 'aromatic' group, this term having been first applied to certain naturally occurring compounds (which were afterwards proved to be benzene-derivatives) on account of their peculiar aromatic odour.

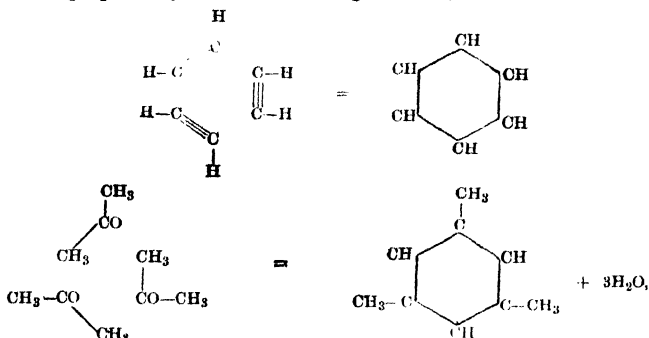
The fundamental distinction between aliphatic and aromatic compounds is one of *structure*. All derivatives of benzene, and all other compounds which contain a *closed-chain* or nucleus *similar* to that of benzene, are classed as aromatic or *benzenoid*. Aliphatic compounds, on the other hand, such as $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3$, $CH_2(OH) \cdot CH(OH) \cdot CH_2(OH)$, and $COOH \cdot CH_2 \cdot CH_2 \cdot COOH$, do not contain a closed-chain, but an *open-chain*¹ of carbon atoms; such compounds, moreover, may be regarded as derived from methane by a series of simple steps.

It must not be supposed, however, that all aromatic compounds are sharply distinguished from all aliphatic or fatty substances, or that either class can be defined in very exact terms. The mere fact that the constitution of a substance must be represented by a closed-chain formula does not make it an aromatic compound; succinimide (p. 248), for example, although it is a closed-chain compound, is clearly a member of the aliphatic series, because of its relationship to succinic acid, into which it is very easily converted. Although, again, the members of the aromatic group may all be regarded as derivatives of benzene, this hydrocarbon and many other aromatic compounds may be directly obtained from members of the fatty series by simple reactions; conversely, many aromatic compounds may be converted into those of the aliphatic series.

Some examples of the production of aromatic, from aliphatic, compounds have already been given—namely, the formation of benzene by the polymerisation of acetylene, and that of mesitylene

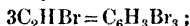
¹ The term 'open-chain' corresponds with the chain-like appearance of the structural formulæ as usually written, and is not intended to convey any idea of the arrangement of the atoms in space (compare p. 46); when the carbon atoms at the ends of the open-chain are united, a closed-chain or ring-compound results.

by the condensation of acetone; these two changes may be expressed graphically in the following manner,

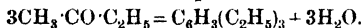


and may be regarded as typical reactions, because many other substances, similar in constitution to acetylene and acetone respectively, may be caused to undergo analogous transformations.

Bromoacetylene, $\text{CBr}:\text{CH}$, for example, is converted into symmetrical tribromobenzene when it is exposed to direct sunlight,



and methylethyl ketone (a homologue of acetone) is transformed into symmetrical triethylbenzene (a homologue of mesitylene or trimethylbenzene) when it is distilled with sulphuric acid,



As examples of the conversion of aromatic into aliphatic compounds the following may be given: Benzene, treated with a mixture of sulphuric acid and potassium chlorate, gives *trichloroacetylacrylic acid*, $\text{CCl}_3\cdot\text{CO}\cdot\text{CH}:\text{CH}\cdot\text{COOH}$, and in the presence of vanadium pentoxide, it can be directly oxidised by free oxygen to maleic acid (p. 256), from which malic acid can be prepared. Benzene combines directly with ozone (3 mols.) and the product is decomposed by water giving glyoxal (p. 219). Phenol, with hydrogen, in the presence of nickel (compare p. 356) gives *cyclohexanol*, $\text{C}_6\text{H}_{11}\cdot\text{OH}$, which, on oxidation is converted, first into *cyclohexanone*, $\text{C}_6\text{H}_{10}\text{O}$, and then into adipic acid, $\text{COOH}\cdot[\text{CH}_2]_4\cdot\text{COOH}$ (p. 261).

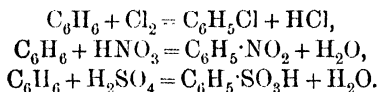
It is also possible to convert an aromatic into an aliphatic compound by direct reduction; salicylic acid (p. 470), for example, is thus transformed into pimelic acid (p. 261).

General Character of Aromatic Compounds.—Although it is impossible to class all organic compounds as either aliphatic or aromatic, because many substances are known which form connecting links between the two groups (p. 519), those which

resemble benzene differ materially from those of the aliphatic division in constitution, and consequently also in properties.

Speaking generally, aromatic compounds contain a larger percentage of carbon than do those of the aliphatic group and are usually crystalline at ordinary temperatures. They are, as a rule, less readily resolved into simple substances than are the members of the aliphatic series (except the very stable paraffins), although in most cases they are more easily converted into substitution products.

Aromatic compounds give substitution products with (1) *halogens*, (2) *nitric acid*, (3) *sulphuric acid*.

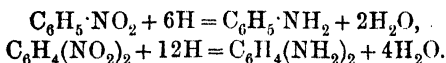


Their behaviour with nitric acid and with sulphuric acid is particularly characteristic, and distinguishes them from nearly all fatty compounds. With concentrated nitric acid, as a rule, they readily give *nitro-derivatives*, and with concentrated sulphuric acid they give *sulphonic acids*.

Aliphatic compounds rarely give nitro- or sulphonic-derivatives under such conditions, but are oxidised and resolved into two or more substances.

The readiness with which the hydrogen atoms of the nucleus are displaced by halogen, NO_2 - or SO_3H -, groups varies very greatly; the hydrocarbons themselves are not very reactive, but when one hydrogen atom of the nucleus has been displaced by particular groups, further substitution often occurs with very great facility. Although halogens, nitric acid and sulphuric acid, are the main reagents by which aromatic compounds are directly changed, it is possible by indirect methods to displace the hydrogen atoms of the nucleus by many other groups such as CH_3 -, HO -, NH_2 -, &c., as will be shown later.

When aromatic nitro-compounds are suitably reduced, they are converted into *amino-compounds*,



These amino-derivatives differ from the aliphatic amines in at least one very important respect, inasmuch as they are converted

into diazonium-compounds (p. 400) on treatment with nitrous acid in the cold; this behaviour is highly characteristic, and the diazonium-compounds form one of the more interesting and important classes of aromatic substances.

When the hydrogen atoms in benzene are displaced by groups or radicals which are composed of several atoms, these groups are spoken of as **side-chains**; the aliphatic groups in *ethylbenzene*, $C_6H_5 \cdot CH_2 \cdot CH_3$, *benzyl alcohol*, $C_6H_5 \cdot CH_2 \cdot OH$, and *methylaniline*, $C_6H_5 \cdot NH \cdot CH_3$, for example, would be called side-chains, whereas the term, as a rule, would not be used in the case of *phenol*, $C_6H_5 \cdot OH$, *nitrobenzene*, $C_6H_5 \cdot NO_2$, &c., where the substituent groups are comparatively simple, and do not contain carbon atoms.

Now the behaviour of any particular atom or group in an aliphatic side-chain, although influenced to some extent by the fact that the group is united with the benzene nucleus, is on the whole very similar to that which it shows in aliphatic compounds. The consequence is that aromatic compounds, containing side-chains of this kind, have not only the properties already referred to as characteristic of the derivatives of benzene, but show also, to a certain extent, the behaviour of aliphatic compounds. *Benzyl chloride*, $C_6H_5 \cdot CH_2Cl$, for example, may be directly converted into the nitro-derivative, $C_6H_4(NO_2) \cdot CH_2Cl$, and the sulphonic acid, $C_6H_4(SO_3H) \cdot CH_2Cl$, reactions characteristic of aromatic compounds. On the other hand, the $-CH_2Cl$ group may be transformed into $-CH_2OH$, $-CHO$, $-COOH$, and so on, just as may the $-CH_2Cl$ group in ethyl chloride, $CH_3 \cdot CH_2Cl$; and in all cases the products retain certain characteristics of aliphatic substances so long as the side-chain remains. The carbon atoms contained in the side-chains, moreover, are generally easily attacked and separated from the rest of the molecule, which constitutes the closed-chain or nucleus; when *ethylbenzene*, $C_6H_5 \cdot CH_2 \cdot CH_3$, or *propylbenzene*, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$, for example, is boiled with chromic acid, the side-chain undergoes oxidation, and benzoic acid, $C_6H_5 \cdot COOH$, is produced in each case; from this acid benzene may be easily obtained, the carbon atoms of the nucleus remaining unchanged during all these transformations.

Although the compounds derived from benzene by direct substitution are very numerous, the aromatic group also includes a

great many other substances, which are more distantly related to benzene, and which can only be regarded as derived from it indirectly. The hydrocarbon *diphenyl*, $\text{C}_6\text{H}_5\text{--C}_6\text{H}_5$, for example, which, theoretically, is formed by the union of two *phenyl*- or $\text{C}_6\text{H}_5\text{--}$ groups, just as dimethyl or ethane, $\text{CH}_3\text{--CH}_3$, is produced by the combination of two methyl-groups, is an important member of the aromatic division, and, like benzene, is capable of yielding a very large number of derivatives. Other hydrocarbons are known in which the presence of two or more closed carbon-chains, combined in different ways, has been proved, as, for example, in the cases of naphthalene (p. 475) and anthracene (p. 492), and there are also substances, such as pyridine (p. 505) and quinoline (p. 513), in which a nitrogen atom occupies the position of one of the $\text{CH}\equiv$ groups in the closed-chain.

All these, and many other different types of compounds, are classed as aromatic, or benzenoid, because they show the general behaviour already referred to, and resemble benzene more or less closely in constitution.

The Reduction of Aromatic Compounds.

It has already been pointed out that benzene does not show the ordinary behaviour of unsaturated aliphatic compounds, but that, under certain conditions, it is capable of forming additive compounds by direct combination with atoms of chlorine or bromine. This fact proves that benzene is not really a saturated compound, like methane or ethane, for example, both of which are quite incapable of yielding derivatives except by substitution. Nevertheless, as a rule, the conversion of benzene and its derivatives into additive products is much less readily accomplished than is that of unsaturated aliphatic compounds; the halogen acids, for example, which unite directly with many unsaturated aliphatic compounds, have no such action on benzene and its derivatives, and even in the case of the halogens, direct combination occurs only under particular conditions.

For these reasons, although benzene was discovered in 1825, very few additive compounds prepared directly from the hydrocarbon or its derivatives were known until a very much later date. In addition to the halogen additive products already mentioned (p. 332) *hexahydrobenzene*, C_6H_{12} (now called *cyclo-*

hexane), had been obtained in small quantities in an impure condition by heating benzene with hydriodic acid at a high temperature (Berthelot), but no satisfactory method for the reduction of the hydrocarbon or of its homologues had been discovered.

The investigations of Sabatier and Senderens (1897–1905) completely altered this state of affairs. These chemists showed that in the presence of certain metals, more especially nickel, *in a particular form* (p. 359), many types of aliphatic compounds combine with hydrogen under suitable conditions; the only noteworthy exceptions are the saturated compounds—the paraffins, their ethers, their amino- and hydroxy-derivatives, and their carboxylic acids. In some cases, as, for example, in that of acetylene, it is only necessary to pass the mixture of the two gases over suitably-prepared nickel at the ordinary temperature. A reaction takes place with the development of heat, and in the presence of a sufficiently large excess of hydrogen, ethane is practically the only product; as a rule, however, a mixture of the vapour of the organic compound and hydrogen is passed over a layer of the catalyst, which is heated at a suitable temperature, usually in the neighbourhood of 130° to 200°. For each particular reaction there is an optimum temperature which is found experimentally, and unless the conditions are suitably chosen the reaction may take a course quite different from that which is expected or desired.

Under suitable conditions, ethylene can be reduced quantitatively to ethane, and other olefines to the corresponding paraffins. Unsaturated alcohols, such as allyl alcohol (p. 230), unsaturated esters, such as ethyl acrylate, and unsaturated acids, such as crotonic acid (p. 234), can be similarly transformed into the corresponding saturated compounds. Other types of aliphatic compounds are likewise reduced; nitriles, for example, give primary, and carbylamines give secondary amines. Aldehydes and ketones are converted into the corresponding primary or secondary alcohols, and in the latter case the products are as a rule free from pinacols (p. 142). Olefinic aldehydes and ketones are generally first reduced to the corresponding paraffin derivatives, which may then be further converted into the saturated primary or secondary alcohols.

In the course of time Sabatier's discovery of the catalytic action of nickel was applied to the 'hardening' of oils (p. 228), a process in which the unsaturated acids, contained as glycerides in natural fats and oils, are converted into saturated compounds.

In other investigations it was shown that benzene combines readily with hydrogen in the presence of the nickel catalyst, and is easily transformed into *hexahydrobenzene*; also that the homologues of benzene and many other types of aromatic compounds can be converted into their hexahydro-derivatives in a similar manner. This discovery made it possible to prepare, not only in the laboratory, but on a large scale, many compounds which, previously, were rarely met with in the study of organic chemistry, and which formed a connecting link between the aromatic and the open-chain aliphatic compounds; such reduction products which still contain a closed-chain of six carbon atoms are derivatives of *cyclohexane*, and belong to the class of *cycloparaffins*.

Aromatic hydrocarbons, other than homologues of benzene, such as naphthalene (p. 475) and anthracene, and other *benzenoid* compounds, can be reduced in a similar manner, and in these cases it is often possible to isolate more than one reduction product; thus from naphthalene either the *tetrahydro*-derivative, $C_{10}H_{12}$, or the *decahydro*-derivative, $C_{10}H_{18}$ (p. 482), can be prepared, according to the temperature employed.

The monohydroxy- and monoamino-substitution products of benzene and its homologues, which are described later, are reduced to the corresponding cyclohexane derivatives; but the bases may be partly transformed into the cyclic hydrocarbons with the formation of ammonia, and other secondary reactions may also take place to a considerable extent. Aromatic carboxylic acids cannot be easily reduced by this method, but the esters of the monocarboxylic acids combine readily with hydrogen, and the products, on hydrolysis, give the corresponding cyclohexane-carboxylic acids.

An aromatic compound, in the molecule of which there is an unsaturated side-chain, may undergo reduction in various stages. Thus, a hydrocarbon containing an unsaturated side-chain, styrene, for example (p. 464), may be reduced first to ethylbenzene (at 300°), and then to ethylcyclohexane (at 180°). Similarly benzaldehyde (p. 437) and acetophenone (p. 444) may be reduced

first to the corresponding aromatic hydrocarbons (toluene and ethylbenzene respectively), and then, by lowering the temperature, to the corresponding cycloparaffins.

When, in using nickel, the temperature is raised above about 250° , the reduction of benzene becomes less complete, and ceases at about 300° ; above this temperature, in the presence of the nickel catalyst, the cyclohexane decomposes into benzene and hydrogen, and a portion of the hydrocarbon is reduced to methane.

The nickel used in the above-described reactions is obtained by dissolving the metal in nitric acid (free from halogen compounds), igniting the nitrate at a dull-red heat until decomposition is complete, and then reducing the oxide in a stream of pure hydrogen at a temperature of about 300° . Another method is to agitate pumice (crushed to pieces of a suitable size) with a paste of well-washed, precipitated nickel hydroxide, and then to heat the dried material in a stream of pure hydrogen until the oxide is partially or completely reduced (compare p. 230).

The metal thus obtained varies in colour from light brown to black; it is frequently pyrophoric, and in any case is readily oxidised on exposure to the air; for this reason the reduction of the oxide is carried out in the tube, which is to be used later in the reduction of the organic compound.

It is of the greatest importance that the hydrogen used in the preparation of the catalyst, and for the reduction of the organic compound, should be pure, or at any rate free from even traces of halogen, sulphur, arsenic, and phosphorus compounds, many of which 'poison' the catalyst and render it useless. Even with pure hydrogen, the presence of traces of compounds of these elements may entirely prevent reduction; thus, benzene containing traces of thiophene (p. 520) cannot be reduced, although the presence of a considerable proportion of carbon disulphide does not prevent the conversion of the hydrocarbon into cyclohexane.

Hydrogen generated from zinc and diluted, pure hydrochloric acid may be purified by passing it through alkaline permanganate, then through a tube containing copper at a dull-red heat, and then through tubes containing moistened alkali; it is not essential to free the gas from water vapour.

The catalyst may be prepared and used in an ordinary combustion tube (p. 19), partly immersed in a layer of sand contained in an iron gutter, one or two thermometers, with their bulbs in the sand, serving to indicate the temperature. If the substance to be reduced is sufficiently volatile, it may be placed in a distillation flask heated at a suitable temperature, and there vaporised in the stream of hydrogen; or it may be dropped from a separating-funnel into the vertical limb of a T-piece, the hydrogen being passed through the horizontal portion. In the latter case, if the liquid is not completely vaporised before it enters the combustion tube, the exit end of the T-piece is lengthened sufficiently

to allow any liquid to drop into a porcelain boat, placed in the combustion tube and heated at a suitable temperature; if the catalyst gets soaked by the liquid its efficiency may be seriously diminished. Readily volatile solids of low melting-point can be treated in the same way, but those of high melting-point or of low volatility are heated in a porcelain boat placed near the inlet of the hydrogen.

CHAPTER XXIII.

HOMOLOGUES OF BENZENE AND OTHER HYDROCARBONS.

BENZENE, the simplest hydrocarbon of the aromatic group, is also the first member of a homologous series of the general formula, C_nH_{2n-6} ; the hydrocarbons of this series are derived from benzene by the substitution of alkyl-groups for hydrogen atoms, just as the homologous series of paraffins is derived from methane. *Toluene* or *methylbenzene*, $C_6H_5 \cdot CH_3$, is the only homologue of the molecular formula, C_7H_8 , but the next higher member, which has the molecular formula, C_8H_{10} , occurs in four isomeric forms—namely, as *ethylbenzene*, $C_6H_5 \cdot C_2H_5$, and as *ortho*-, *meta*-, and *para*-*dimethylbenzene*, $C_6H_4(CH_3)_2$; higher up the series, the number of theoretically possible isomerides rapidly increases. By the substitution of a methyl-group for one atom of hydrogen in the hydrocarbons, C_8H_{10} , for example, eight isomerides of the composition, C_9H_{12} , may theoretically be obtained, and are, in fact, known (p. 342).

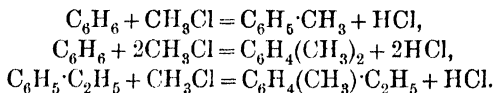
Owing to this rapid increase in the number of isomerides, as the series is ascended, and to the differences in the properties of these isomerides, but more especially because, as a rule, only the lower members are of much importance, the classification of aromatic compounds into various homologous series does not very much simplify their study; nevertheless *general* methods of preparation may be given and also the general properties of particular groups present in the molecules of the homologues.

Many of the hydrocarbons of the C_nH_{2n-6} series, and others which will be mentioned later, occur in coal-tar, from which they are extracted; it is, however, very difficult to obtain any of them in a pure state directly from this source, by fractional distillation

alone, as the boiling-points of some of the isomerides lie very close together and also differ very little from those of certain other types of compounds which are present.

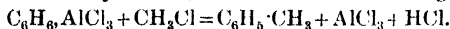
The homologues of benzene may be obtained by the following general methods:

(1) Benzene (or one of its homologues) is treated with an alkyl halogen compound in the presence of anhydrous aluminium chloride (*Friedel and Crafts' reaction*); under these conditions the hydrogen atoms of the nucleus are displaced by alkyl-groups, benzene and methyl chloride, for example, giving *toluene*, $C_6H_5 \cdot CH_3$, *xylylene*, $C_6H_4(CH_3)_2$, *trimethylbenzene*, $C_6H_3(CH_3)_3$, &c.; whereas *ethylbenzene*, with the same alkyl compound, yields *methylethylbenzene*, $C_6H_4(CH_3) \cdot C_2H_5$, *dimethylethylbenzene*, $C_6H_3(CH_3)_2 \cdot C_2H_5$, and so on,



Anhydrous benzene, or one of its homologues (1 part),¹ is placed in a flask connected with a reflux condenser, and *anhydrous* aluminium chloride (about $\frac{1}{3}$ part) is added; the apparatus and materials must be dry, and it is essential that the aluminium chloride should be of good quality (samples which have absorbed atmospheric moisture, and which look white and powdery, are practically useless). The theoretical quantity of the alkyl halide is then passed or dropped into the hydrocarbon, and the mixture is afterwards heated on a water-bath until the evolution of halogen acid is at an end. In some cases, ether, carbon disulphide, or petroleum is mixed with the original hydrocarbon in order to dilute it. When the product is quite cold, water is gradually added to it in order to dissolve the aluminium compounds, and after having been separated, and dried with calcium chloride, the mixture of hydrocarbons is submitted to fractional distillation; in some cases a preliminary distillation in steam is advisable.

It is probable that an aluminium compound, such as $C_6H_5 \cdot AlCl_3$, is first formed, and in reactions using acid chlorides (p. 444), addition compounds, $R \cdot COCl \cdot AlCl_3$, have actually been isolated; these substances then react with the alkyl halide, aluminium chloride being regenerated,

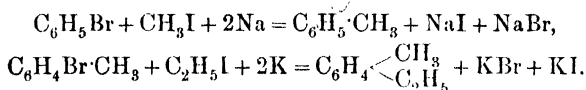


Anhydrous ferric or zinc chloride may be employed in the place of aluminium chloride, but, as a rule, not so successfully.²

¹ In this and other subsequent preparations, the 'parts' are by weight and the actual quantities taken will depend on the amount of product required.

² Friedel and Crafts' reaction is also applicable to phenolic ethers (p. 426), but not, as a rule, to other derivatives of aromatic hydrocarbons.

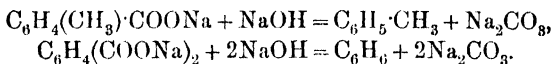
(2) An ethereal solution of a halogen derivative of benzene or of one of its homologues and an alkyl halogen compound, is heated with sodium or potassium (*Fittig's reaction*); this method of formation is similar to that by which the higher paraffins may be synthetically produced from methane (compare Wurtz reaction, p. 53), and has the great advantage over Friedel and Crafts' method that the constitution of the product is known. *Bromobenzene* and methyl iodide, for example, give *toluene*, whereas *o*-, *m*-, and *p*-*bromotoluene* and ethyl iodide yield *o*-, *m*-, and *p*-*ethylmethylbenzene* respectively,



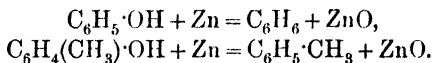
The bromo- or iodo-derivatives of the aromatic hydrocarbons are usually employed because the chloro-derivatives do not react so readily; the alkyl iodides are also used in preference to the chlorides or bromides because they undergo change most easily.

The first stage seems to be the formation of a sodium alkyl compound, $\text{RI} + 2\text{Na} = \text{RNa} + \text{NaI}$, which then, with the aromatic halide, forms the hydrocarbon.

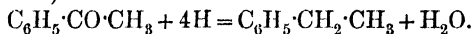
(3) The carboxy-derivatives of benzene, or of its homologues, are heated with soda-lime, a method analogous to that employed for the conversion of the fatty acids into paraffins (p. 50),



(4) The vapour of a hydroxy-derivative of benzene, or of one of its homologues, is passed over strongly heated zinc-dust,



(5) A ketone or aldehyde is reduced by the *Clemmensen* method (p. 143).



(6) Coal, wood, peat, &c., are submitted to destructive distillation, or the vapour of some aliphatic compound is passed through a strongly heated tube (compare p. 330).

General Properties.—Most of the homologues of benzene are colourless, mobile liquids; one or two, however, are crystalline at ordinary temperatures. They all distil without decomposing, are

volatile in steam, and burn with a smoky flame; they are insoluble in water, but miscible with (anhydrous) alcohol, ether, petroleum, &c., in all proportions; they dissolve fats and many other substances which are insoluble in water.

Just as in other homologous series, the homologues of benzene show a gradual variation in *physical properties* with increasing molecular weight, but owing to the large number of isomerides, this is obvious only when *corresponding* compounds are compared, as, for example, the following *mono*-substitution products:

Benzene, C_6H_6	Sp. gr. at 0° 0·899	B.p., 80·2°
Toluene, C_7H_8	" 0·882	" 110·3°
Ethylbenzene, C_8H_{10}	" 0·883	" 136°
Propylbenzene, C_9H_{12}	" 0·881	" 158°

There are, however, three hydrocarbons isomeric with ethylbenzene (p. 360) and seven isomeric with propylbenzene (p. 342), so that after toluene the homologous series branches into a number of such series, and the gradual variation in properties is obscured. Isomeric *di*-substitution products usually differ in physical properties, but the extent of this difference is rather variable; the three xylenes, $C_6H_4(CH_3)_2$, for example, have the following constants:

	Orthoxylene.	Metaxylene.	Paraxylene.
Sp. gr. at 0°	0·893	0·881	0·880
B.p.	146°	139°	138° (m.p. 14°)

As a general rule, to which, however, there are many exceptions, para-compounds melt at a higher temperature than the corresponding meta-compounds, and the latter usually melt at a higher temperature than the corresponding ortho-compounds. This applies to all benzene derivatives, not to hydrocarbons only.

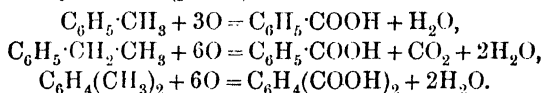
The homologues of benzene show the characteristic chemical behaviour of the parent hydrocarbon, inasmuch as they readily yield halogen-, nitro-, and sulphonic-derivatives; toluene, for example, gives *chlorotoluene*, $C_6H_4(CH_3) \cdot Cl$, *nitrotoluene*, $C_6H_4(CH_3) \cdot NO_2$, and *toluenesulphonic acid*, $C_6H_4(CH_3) \cdot SO_3H$; xylene yields *chloroxylylene*, $C_6H_3(CH_3)_2 \cdot Cl$, *nitroxylene*, $C_6H_3(CH_3)_2 \cdot NO_2$, and *xylenesulphonic acid*, $C_6H_3(CH_3)_2 \cdot SO_3H$.

In these, and in all similar reactions, the product invariably consists of a mixture of isomerides, and the course of the reaction depends both on the nature of the aromatic compound and on the conditions of the experiment (compare p. 381); as

a rule, the greater the number of alkyl-groups in the hydrocarbon, the more readily does it yield halogen-, nitro-, and sulphonic-derivatives.

The fact that benzene and its homologues gradually dissolve in concentrated sulphuric acid is sometimes made use of for the separation of these aromatic hydrocarbons from the paraffins, as, for example, in the analysis of coal-gas; their separation from *unsaturated* hydrocarbons could not of course be accomplished in this way, as the latter are attacked by concentrated sulphuric acid, giving soluble hydrogen sulphates.

All the homologues of benzene are very stable, and are with difficulty resolved into compounds containing a smaller number of carbon atoms; powerful oxidising agents, however, such as chromic acid, potassium permanganate, and *dilute* nitric acid, act on them slowly, the alkyl-groups or side-chains being attacked, and, as a rule, converted into carboxyl-groups; toluene and ethylbenzene, for example, give benzoic acid, whereas the xylenes yield dicarboxylic acids (p. 456),



Although in most cases oxidation leads to the formation of a carboxy-derivative of benzene, the stable benzene nucleus remaining unchanged, some of the homologues are completely oxidised to carbon dioxide and water (compare p. 367), and benzene itself undergoes a similar change on prolonged and vigorous treatment.

In the case of aromatic, as in that of aliphatic compounds, it is convenient to give names to certain groups of atoms or *radicals*; the mono- and di-substitution products of benzene, for example, may be regarded as compounds of the univalent radical, *phenyl*, C_6H_5- , or **Ph**, and of the bivalent radical, *phenylene*, $\text{C}_6\text{H}_4<$, respectively, as in *phenylamine* (aniline), $\text{C}_6\text{H}_5\cdot\text{NH}_2$, and in *o*-, *m*-, and *p*-*phenylenediamine*, $\text{C}_6\text{H}_4(\text{NH}_2)_2$. Toluene derivatives, again, may be named as if they were derived from the radical, *tolyl*, $\text{CH}_3\cdot\text{C}_6\text{H}_4-$, or from the radical, *benzyl*, $\text{C}_6\text{H}_5\cdot\text{CH}_2-$, according as hydrogen of the nucleus, or of the side-chain, has been displaced. The compound, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{OH}$, for example, is called *benzyl alcohol*; the isomeric hydroxy-toluenes, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{OH}$, however, are usually known as the (**o.m.p.**) *cresols* (p. 429) and not as *tolyl alcohols*.

Radicals derived from aromatic hydrocarbons are termed **aryl radicals**.

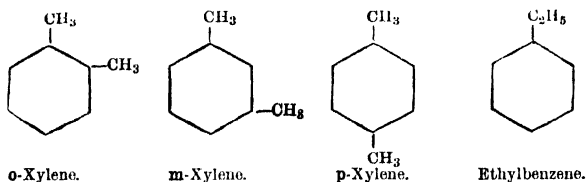
Toluene, $C_6H_5 \cdot CH_3$ (methylbenzene, phenylmethane), is prepared commercially from the '90 per cent. benzol' separated from coal-tar (p. 327), and from certain varieties of petroleum; it may be obtained by heating toluic acid with soda-lime (p. 450), or by any of the other general reactions given above; also by the dry distillation of balsam of Tolu (hence the name toluene) and other resins.

Commercial coal-tar toluene (toluol) is impure, and when shaken with concentrated sulphuric acid it colours the acid brown or black. Even after repeated fractional distillation, it contains *methylthiophene*, C_5H_6S , a homologue of thiophene (p. 520), and shows the indophenin reaction (with isatin and concentrated sulphuric acid).

Toluene is a mobile liquid of sp. gr. 0.882 at 0° , boiling at 111° ; it does not solidify even at -28° , and cannot, therefore, like benzene, be easily purified by crystallisation. It resembles benzene very closely in most respects, and differs from it principally in those properties which are due to the presence of the methyl-group. Its behaviour with nitric acid and with sulphuric acid, for example, is similar to that of benzene, inasmuch as it yields nitro- and sulphonic-derivatives; these compounds, moreover, exist in three isomeric (o.m.p.) forms, since they are di-substitution products of benzene. The presence of the methyl-group, on the other hand, causes toluene to show in some respects the properties of a paraffin. The hydrogen of this methyl-group may be displaced by chlorine, for example, and the latter by a hydroxyl- or amino-group, by methods exactly similar to those employed in bringing about corresponding changes in aliphatic compounds; substances such as $C_6H_5 \cdot CH_2Cl$, $C_6H_5 \cdot CH_2 \cdot OH$, and $C_6H_5 \cdot CH_2 \cdot NH_2$, are thus obtained. This behaviour, perhaps, was to be expected, since toluene or phenylmethane is a mono-substitution product of methane just as much as a derivative of benzene. Toluene is a most important compound and is employed in the manufacture of various dye-intermediates described later, explosives, and saccharin (p. 455); it is also used as a fuel for internal combustion engines—usually in admixture with benzene and petrol.

Xylenes.—There are four hydrocarbons of the molecular

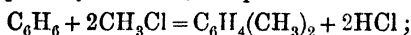
formula, C_8H_{10} (the next homologues of toluene), of which the three *xylenes* or dimethylbenzenes are the more important :



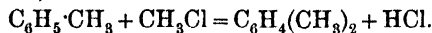
The three *xylenes* occur in coal-tar, and may be partially separated from the other components of '50 per cent. benzol' (p. 327) by fractional distillation. The portion which, after repeated distillation, boils at $138-142^\circ$, contains a large quantity (usually about 60 per cent.) of *m*-xylene and smaller quantities of the *o*- and *p*-compounds; the three isomerides cannot be separated from one another (or from all impurities) by further distillation, or by any simple means, although it is possible to obtain a complete separation by taking advantage of differences in their chemical behaviour.

m-Xylene is readily separated from the other isomerides with the aid of boiling dilute nitric acid, which oxidises *o*- and *p*-xylene to the corresponding toluic acid, $C_6H_4(CH_3) \cdot COOH$, but does not readily attack *m*-xylene; the product is rendered alkaline, and the unchanged hydrocarbon is purified by distillation in steam and fractionation. The isolation of *o*- and *p*-xylene depends on the following facts: (1) When crude xylene is agitated with concentrated sulphuric acid, *o*- and *m*-xylene are converted into sulphonic acids, $C_6H_3(CH_3)_2 \cdot SO_3H$; *p*-xylene remains undissolved, as it is only slowly acted on even by anhydrosulphuric acid. (2) The sodium salt of *o*-xylenesulphonic acid is less soluble in water than the sodium salt of *m*-xylenesulphonic acid; it is purified by recrystallisation and heated with hydrochloric acid under pressure, whereby it is converted into *o*-xylene.

The three *xylenes* may all be prepared by one or other of the general methods; when, for example, methyl chloride is passed into benzene in the presence of aluminium chloride, *m*-xylene and a small quantity of the *p*-compound are obtained,



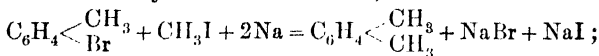
toluene, under the same conditions, yields, of course, the same two compounds,



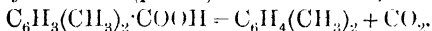
The non-formation of *o*-xylene in these two reactions shows that

the methyl-group first introduced into the benzene molecule exerts some directing or *orientating influence* on the position taken up by the second one (p. 382).

o-Xylene is obtained in a state of purity by treating *o*-bromotoluene with methyl iodide and sodium,

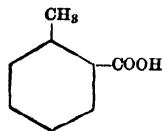


pure *p*-xylene is produced in a similar manner from *p*-bromotoluene; *m*-xylene might be obtained by treating *m*-bromotoluene with methyl iodide and sodium, but is more easily prepared by heating mesitylenic acid (p. 368) with soda-lime,

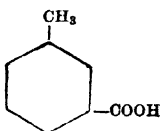


These isomerides may also be obtained by treating the respective Grignard compounds of the bromotoluenes with dimethyl sulphate.

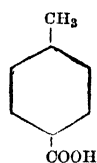
The three xylenes are very similar in physical properties (compare p. 363), and are all mobile, rather pleasant-smelling, inflammable liquids (*p*-xylene melts at 14°), which distil without decomposing, and are readily volatile in steam. They also resemble one another in chemical properties, although in some respects they show very important differences.¹ On oxidation, under suitable conditions, they are all converted in the first place into monocarboxylic acids, represented respectively by the formulæ,



o-Toluic Acid.



m-Toluic Acid.



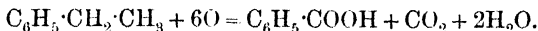
p-Toluic Acid.

On further oxidation the second methyl-group undergoes a like change, and the three corresponding dicarboxylic acids, $\text{C}_6\text{H}_4(\text{COOH})_2$, are formed (p. 456).

The three hydrocarbons show, however, a marked dissimilarity towards oxidising agents. With chromic acid, *o*-xylene is completely oxidised to carbon dioxide and water, whereas *m*- and *p*-xylene yield the dicarboxylic acids, results very different from those obtained with dilute nitric acid (p. 366). The behaviour of the three hydrocarbons towards sulphuric acid is also different (p. 366).

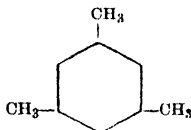
¹ The xylenes, like other isomerides, afford further examples of the fact that the properties of a compound are not entirely determined by those of its constituent groups but by the structure of the molecule as a whole.

Ethylbenzene, $C_6H_5 \cdot C_2H_5$ (phenylethane), an isomeride of the xylenes, is not of much importance; it occurs in coal-tar, and may be obtained by the general methods. It boils at 136° , and, on oxidation with dilute nitric acid or chromic acid, it is converted into benzoic acid,

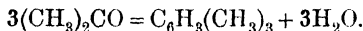


The next member of the series has the molecular formula, C_9H_{12} , and exists, as already pointed out (p. 342), in eight isomeric forms, of which the three trimethylbenzenes and isopropylbenzene are the more important.

Mesitylene, 1:3:5-, or symmetrical, trimethylbenzene,



occurs in small quantities in coal-tar, but is best prepared by distilling a mixture of acetone (2 vols.), concentrated sulphuric acid (2 vols.), and water (1 vol.), and then fractionating the distillate,



The formation of mesitylene in this way is of interest, not only because it affords a means of synthesising the hydrocarbon from its elements, but also because it throws light on the constitution of the compound (p. 353).

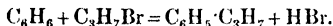
Although the change is most simply expressed by the graphic equation already given (p. 353), it might be assumed that the acetone is first converted into $CH_3 \cdot C(OH) : CH_2$ (by isomeric change), or into $CH_3 \cdot C : CH$, and that mesitylene is then produced by a secondary reaction. Whatever view, however, is adopted, as to the various stages of the reaction (unless, indeed, highly improbable assumptions are made), it would seem that the constitution of the product must be expressed by a *symmetrical* formula; this inference has been fully confirmed by other evidence (p. 350).

Mesitylene is a colourless, mobile, pleasant-smelling liquid, boiling at 164.5° , and volatile in steam; when treated with concentrated nitric acid, it yields *mononitro-* and *dinitro-mesitylene*, whereas with a mixture of nitric and sulphuric acids it is converted into *trinitromesitylene*, $C_6(NO_2)_3(CH_3)_3$. On oxidation with dilute nitric acid, it yields *mesitylenic acid*,

$C_6H_3(CH_3)_2 \cdot COOH$, *uritic acid*, $C_6H_3(CH_3)(COOH)_2$, and *trimesic acid*, $C_6H_3(COOH)_3$, by the successive transformation of methyl- into carboxyl-groups.

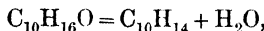
Pseudocumene, or 1:2:4-trimethylbenzene, and hemimellitene, or 1:2:3-trimethylbenzene, also occur in small quantities in coal-tar, and are very similar to mesitylene in properties; on oxidation, they yield various acids by the conversion of one or more methyl- into carboxyl-groups.

Cumene, $C_6H_5 \cdot CH(CH_3)_2$ (isopropylbenzene), is usually obtained from coal-tar; it may be prepared by treating a mixture of isopropyl bromide and benzene with aluminium chloride,

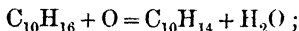


It boils at 153° and, on oxidation with dilute nitric acid, it is converted into benzoic acid.

Cymene, $C_6H_4(CH_3) \cdot C_3H_7$ (*p*-methylisopropylbenzene), is a hydrocarbon of considerable importance, and occurs in the ethereal oils or essences of many plants; it may be obtained in many ways, as, for example, by heating camphor with phosphorus pentoxide,

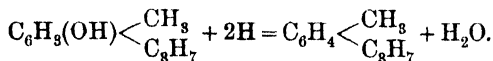


and by heating oil of turpentine with concentrated sulphuric acid,



very complex changes take place in both these reactions.

Also by heating thymol or carvacrol (p. 430), with phosphorus pentasulphide (which acts as a reducing agent),



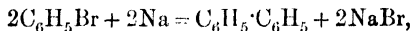
It has been synthesised from *p*-bromoisopropylbenzene, methyl iodide, and sodium—a reaction which proves its constitution.

Cymene is a pleasant-smelling liquid of sp. gr. 0.8722 at 0° , and boils at 175 – 176° ; on oxidation with dilute nitric acid, it yields *p*-toluic acid, $C_6H_4(CH_3) \cdot COOH$, and *terephthalic acid*, $C_6H_4(COOH)_2$.

Diphenyl, Diphenylmethane, and Triphenylmethane.

All the hydrocarbons hitherto described contain only *one* benzene nucleus, and may be regarded as derived from benzene by the substitution of alkyl-groups for atoms of hydrogen; there are, however, several other types of aromatic hydrocarbons, which include compounds of considerable importance.

Diphenyl, $C_6H_5-C_6H_5$, is not a homologue of benzene, and its molecule contains *two* benzene nuclei. It is formed by treating an ethereal solution of bromobenzene with sodium,



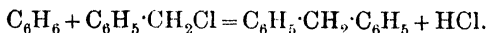
a reaction which is analogous to the formation of ethane (dimethyl) from methyl iodide (p. 53), but many other changes occur and the yield is very poor; it is also produced in the preparation of magnesium phenyl bromide (p. 380).

Diphenyl is prepared on the large scale by passing benzene vapour through molten lead, $2C_6H_6 = C_6H_5 \cdot C_6H_5 + H_2$. The product is fractionated, and the diphenyl is purified by distillation and recrystallisation.

Diphenyl is colourless, melts at 71° , and boils at 254° ; when oxidised with chromic acid it yields benzoic acid, $C_6H_5 \cdot COOH$, one of the benzene nuclei giving rise to $-COOH$. Its behaviour with halogens, nitric acid, and sulphuric acid is similar to that of benzene, substitution products being formed.

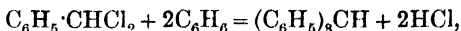
Diphenylmethane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$, also contains *two* benzene nuclei; it may be regarded as derived from methane by the substitution of two phenyl-groups for two atoms of hydrogen, just as toluene or phenylmethane may be considered as a mono-substitution product of methane.

Diphenylmethane may be prepared by treating benzene with benzyl chloride (p. 378) in the presence of aluminium chloride,

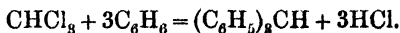


It is crystalline, and melts at 26.5° ; when treated with nitric acid, it yields nitro-derivatives in the usual way, and on oxidation with chromic acid, it is converted into diphenyl ketone or *benzophenone*, $C_6H_5 \cdot CO \cdot C_6H_5$ (p. 445).

Triphenylmethane, $(C_6H_5)_3CH$, is the parent substance of an important group of compounds, all of which contain *three* benzene nuclei. It is formed when benzal chloride (p. 379) is treated with benzene in the presence of aluminium chloride,



and also when a mixture of chloroform and benzene is warmed with aluminium chloride,



Triphenylmethane is colourless, melts at 92° , and boils at 358° ; it is readily soluble in ether and benzene, but only sparingly so in cold alcohol. When treated with fuming nitric acid, it is converted into a yellow, crystalline *trinitro*-derivative, $\text{CH}(\text{C}_6\text{H}_4\cdot\text{NO}_2)_3$, which, like other nitro-compounds, is readily reduced to the corresponding *triamino*-compound, $\text{CH}(\text{C}_6\text{H}_4\cdot\text{NH}_2)_3$; many derivatives of this base are employed as dyes.

On oxidation with chromic acid, triphenylmethane is converted into *triphenyl carbinol*, $(\text{C}_6\text{H}_5)_3\text{C}\cdot\text{OH}$ (m.p. 163°), a compound which can also be obtained by treating benzophenone (p. 445) or ethyl benzoate (p. 451) with magnesium phenyl bromide.

CHAPTER XXIV.

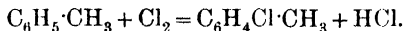
HALOGEN DERIVATIVES OF BENZENE AND OF ITS HOMOLOGUES.

THE action of chlorine and bromine on benzene has already been mentioned (p. 332). At ordinary temperatures, in the absence of direct sunlight, *substitution* products are slowly formed; this action is greatly hastened by the presence of a halogen carrier, such as iodine, iron, aluminium, &c.¹ In the presence of direct sunlight, however, or in the dark in the complete absence of water, the hydrocarbon yields *additive* compounds by direct combination with six atoms of the halogen (p. 332).

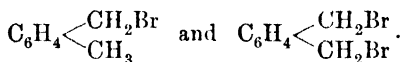
The homologues of benzene also show a notable behaviour; when treated with chlorine or bromine at ordinary temperatures in the absence of direct sunlight, they are converted into *substitution* products by the displacement of hydrogen of the *nucleus*, and, as in the case of benzene itself, the reaction is greatly promoted by the presence of a halogen carrier; under these con-

¹ The action of iodine has already been referred to (p. 164); iron, aluminium, antimony, and certain other metals act as halogen carriers, possibly because their chlorides (FeCl_3 , AlCl_3 , SbCl_5) react with the hydrocarbons and give products, which are then decomposed by the free halogen, with formation of the metallic chloride and a halogen substitution product of the hydrocarbon.

ditions toluene, for example, gives a mixture of *o*- and *p*-chloro-toluenes or bromotoluenes,

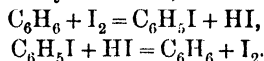


When, on the other hand, no halogen carrier is present, and the hydrocarbons are treated with chlorine or bromine at their boiling-points, or in direct sunlight, they yield derivatives by the displacement of hydrogen of the *side-chain*; when, for example, chlorine is passed into *boiling* toluene, the three hydrogen atoms of the methyl-group are successively displaced, *benzyl chloride*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\text{Cl}$, *benzal chloride*, $\text{C}_6\text{H}_5\cdot\text{CHCl}_2$, and *benzotrichloride*, $\text{C}_6\text{H}_5\cdot\text{CCl}_3$, being formed; xylene, again, when heated at its boiling-point and treated with bromine, gives the compounds,



Although these statements are true in the main, it must not be supposed that, under any conditions, substitution takes place *only* in the nucleus or in the side-chain, as the case may be, because this is not so; in the presence of a halogen carrier, relatively small quantities of halogen derivatives are formed by the displacement of hydrogen of the side-chain, and at the boiling-point of the hydrocarbon, or in direct sunlight, hydrogen of the nucleus is displaced to some extent.

Iodine, as a rule, does not act on aromatic hydrocarbons, and if at high temperatures substitution occurred, the product would be reduced again to the hydrocarbon,



When, however, iodic acid, or some other substance which decomposes hydrogen iodide, is present, iodo-derivatives may sometimes be prepared by direct treatment with the halogen at high temperatures.

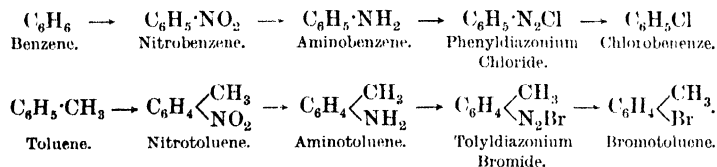
Preparation.—(1) Chloro- and bromo-derivatives of benzene and of its homologues may be prepared by the direct action of chlorine and bromine on the hydrocarbons; such processes in which hydrogen is displaced by the use of the *free halogen* are termed '*chlorination*' or '*bromination*' as the case may be. The conditions to be maintained depend, as explained above, on whether hydrogen of the nucleus or of the side-chain is to be displaced. If, for example, toluene is to be converted into *p*-chlorobenzyl chloride, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{CH}_2\text{Cl}$, the hydrocarbon might be first treated with

chlorine at ordinary temperatures in the presence of iodine; the *p*-chlorotoluene, $C_6H_4Cl \cdot CH_3$, thus formed (after having been separated from the accompanying ortho-compound), would then be boiled in a flask connected with a reflux condenser, and a stream of dry chlorine led into it.

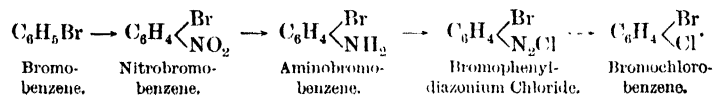
In all operations of this kind the theoretical quantity, or a slight excess of halogen, is employed. Bromine is weighed directly, but in the case of chlorine the process of chlorination is continued until the theoretical gain in weight has taken place; the halogen should be dried, as, in the presence of water, oxidation products of the hydrocarbon may be formed.

(2) A very important general method for the preparation of aromatic halogen derivatives, *containing the halogen combined with carbon of the nucleus*, consists in the decomposition of the diazonium-salts. As the properties and decompositions of the last-named substances are described later (p. 400), it is only necessary to state here that this method is used in the preparation of nearly *all* iodo-compounds, and that it affords a means of indirectly substituting any of the halogens, not only for hydrogen, but also for nitro- or amino-groups.

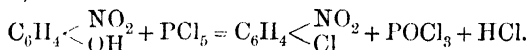
The conversion of benzene or toluene, for example, into a mono-halogen derivative by this method involves the following steps:



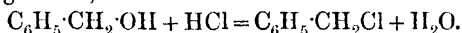
The preparation of a *di*-halogen derivative may sometimes be carried out in a similar manner, the hydrocarbon being first converted into the *di*-nitro-derivative; in most cases, however, it is necessary to prepare the *mono*-halogen derivative by the reactions given above, to convert the latter into the nitro-compound, and then to displace the nitro-group by a halogen atom in the prescribed manner:



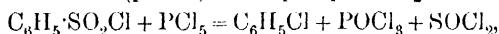
(3) Halogen derivatives of benzene and its homologues are sometimes obtained by treating phenols (p. 425) with the tri- or penta-halogen derivatives of phosphorus, but the main reactions are similar to those which occur in the case of aliphatic hydroxy-compounds;¹ phenols which contain a nitro-group in the *o*- or *p*-position, however, often give a good yield of the corresponding chloronitro-derivative,



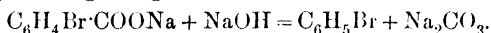
An aromatic alcohol (p. 435), such as benzyl alcohol, may also give the corresponding halogen derivative (*benzyl chloride*), with a phosphorus halide, but usually much better results are obtained with a halogen acid,



(4) Halogen derivatives may also be obtained by heating sulphonyl chlorides (p. 417) with phosphorus pentachloride,



and (5) by heating halogen acids with soda-lime,



Properties.—At ordinary temperatures, most of the *mono*-halogen derivatives of benzene and its simpler homologues are colourless liquids; the *di*- and *tri*-halogen derivatives, however, are generally crystalline. They are all insoluble, or nearly so, in water, but soluble in alcohol, ether, &c. Many are readily volatile in steam, and also distil without decomposing, the boiling-point being higher, and the specific gravity greater, than that of the parent hydrocarbon, and rising as bromine is substituted for chlorine, or iodine for bromine.

	Benzene.	Chlorobenzene.	Bromobenzene.	Iodobenzene.
B.p.	80·2°	132°	156°	188°
Sp. gr. at 0° . .	0·899	1·128	1·517	1·857

They are not so inflammable as the hydrocarbons, and the vapours of many of them (p. 380) have a very irritating action on the eyes and respiratory organs.

When the halogen is united with carbon of the benzene nucleus, it is, as a rule, very firmly combined, and *cannot be displaced by the hydroxyl- or amino-group, with the aid of aqueous alkalis, moist silver oxide, or alcoholic ammonia.* Such halogen derivatives,

¹ Compare footnote, p. 99.

moreover, cannot be converted into less saturated compounds by *alcoholic potash*, in the same way as ethyl bromide, for example, may be converted into ethylene; in fact, no benzenoid compound containing less than six univalent atoms, or their valency equivalent, is known. If, however, hydrogen of the nucleus has been displaced by one or more nitro-groups, as well as by a halogen, the latter often becomes much more open to attack; *o*- and *p*-chloronitrobenzene, $C_6H_4Cl \cdot NO_2$, for example, are moderately easily changed by alcoholic potash and by alcoholic ammonia at high temperatures, yielding the corresponding nitro-phenols, $C_6H_4(OH) \cdot NO_2$, and nitroanilines, $C_6H_4(NH_2) \cdot NO_2$, respectively; *m*-chloronitrobenzene, however, is not changed under these conditions, a fact which shows that such isomerides sometimes differ very considerably in chemical properties (footnote, p. 367).

Halogen atoms of the side-chains are very much less firmly combined than are those of the nucleus, and may be displaced by hydroxyl- or amino-groups just as in aliphatic compounds; *benzyl chloride*, $C_6H_5 \cdot CH_2Cl$, for example, is converted into *benzyl alcohol*, $C_6H_5 \cdot CH_2 \cdot OH$, by boiling sodium carbonate solution, and when heated with alcoholic ammonia, it yields *benzylamine*, $C_6H_5 \cdot CH_2 \cdot NH_2$ (p. 399).

Halogen atoms of the nucleus, as well as those of the side-chain, are displaced by hydrogen with the aid of hydriodic acid and red phosphorus at high temperatures, or of sodium amalgam and aqueous alcohol; the former, however, are much less readily displaced than the latter.

Chlorobenzene, C_6H_5Cl (phenyl chloride), may be described as a typical example of those halogen derivatives in which the halogen is combined with carbon of the nucleus. It may be prepared by Sandmeyer's reaction—that is to say, by treating an aqueous solution of phenyldiazoniumchloride with cuprous chloride (p. 402); this method, therefore, affords a means of preparing chlorobenzene, not only from the diazonium-salt, but also indirectly from aminobenzene (aniline), nitrobenzene, and benzene, in the manner already indicated (p. 373).

Aniline (20 g.) is *diazotised* by the method described on p. 403. To the solution of the diazonium chloride a cold solution of cuprous chloride (10 g.) in concentrated hydrochloric acid (about 100 c.c.) is cautiously added, and the mixture is kept during about twelve hours; the chlorobenzene is then distilled in steam, washed with a solution of sodium hydroxide, separated, dried, and distilled.

On the large scale chlorobenzene is obtained, together with *o*- and *p*-dichlorobenzenes, $C_6H_4Cl_2$, trichlorobenzenes, $C_6H_3Cl_3$, &c., by *chlorinating* benzene in the presence of a carrier (iron), and fractionating the product. It should be noted that chlorobenzene and other *nuclear* halogen derivatives, unlike the alkyl halides, *cannot* be prepared by treating the corresponding hydroxy-compounds (phenols) with a halogen acid.

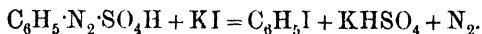
Chlorobenzene is a colourless, mobile, pleasant-smelling liquid; it boils at 132° , and is readily volatile in steam. Like benzene, it is capable of yielding nitro-, amino-, and other derivatives; it *differs* from the alkyl halides in being unchanged by water, boiling alkalis, moist silver oxide, metallic salts, and alcoholic ammonia, but with sodium hydroxide solution in an autoclave at 300° it gives phenol.

Bromobenzene, C_6H_5Br (phenyl bromide), may be prepared from phenyldiazonium sulphate by Sandmeyer's reaction, using cuprous bromide (p. 402); also by *brominating* benzene in the presence of iron.

Benzene (1 part, say 10 g.),¹ together with bright iron wire (about 0.2 g.) is placed in a flask provided with a reflux condenser, and the bromine (2 parts)² is added gradually from a stoppered funnel, the bent stem of which passes through the cork of the flask; the hydrogen bromide which is evolved may be absorbed in a tower containing moist coke. The product is washed well with water and dilute caustic soda successively, dried, and fractionated. The *p*-dibromobenzene (m.p. 89° ; b.p. 219°), which may be formed in the above reaction, remains as a residue if the distillation is continued only until the thermometer rises to about 170° ; it solidifies when cold, and may be recrystallised from aqueous alcohol.

Bromobenzene boils at 155° .

Iodobenzene, C_6H_5I (phenyl iodide), cannot be obtained by the action of iodine alone on benzene (p. 372); it is most conveniently prepared by decomposing phenyldiazonium sulphate with potassium iodide in aqueous solution,



Aniline (1 part)¹ is *diazotised* with sodium nitrite and sulphuric acid (compare p. 403), the cold solution of the diazonium sulphate is treated with a concentrated solution of potassium iodide ($2\frac{1}{2}$ parts), and the

¹ Compare footnote (p. 361).

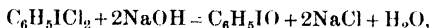
² Very great care must be taken with this dangerous liquid, and the operation should be carried out in a fume chamber.

mixture is gradually heated until nitrogen is no longer evolved; the iodobenzene is then separated by steam distillation, washed with dilute caustic soda, dried, and distilled.

Iodobenzene boils at 188°.

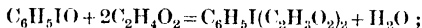
The variation in the physical properties of chloro-, bromo-, and iodo-benzene (p. 374) should be noted; as the halogen atoms in these compounds are so firmly combined, these and other nuclear halogen derivatives of benzene, unlike the alkyl halides, are little used as reagents, except for the preparation of *aryl* Grignard compounds (p. 380).

Iodobenzene dichloride, $C_6H_5 \cdot ICl_2$, separates in crystals when iodobenzene is dissolved in chloroform and dry chlorine is passed into the *well-cooled* solution. It is slowly decomposed by dilute caustic soda (4.5 per cent.), and in the course of 6–8 hours at ordinary temperatures, it is converted into *iodosobenzene*,

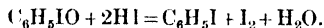


which can be separated by filtration, washed with water, and dried on porous earthenware.

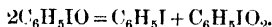
Iodosobenzene, C_6H_5IO , is a colourless solid, moderately easily soluble in warm water and alcohol; it explodes at about 210°. It has *basic* properties, and reacts with acids, forming a salt and water,



it is also an oxidising agent, and liberates iodine from potassium iodide in acid solution,

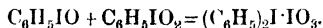


When iodosobenzene is submitted to distillation in steam, it undergoes a most interesting decomposition, giving iodobenzene, which distils over with the water, and *iodoxybenzene*, which is non-volatile,



Iodoxybenzene, $C_6H_5IO_2$, separates in colourless needles when the aqueous solution is evaporated to a small volume and then allowed to cool; it explodes at about 230°. Unlike iodosobenzene, it does not show basic properties, but it is an oxidising agent and liberates iodine (4 atoms) from hydrogen iodide.

When a mixture of iodosobenzene and iodoxybenzene is shaken with water and freshly precipitated silver oxide, interaction takes place and **diphenyliodonium iodate** is formed,



This product is the salt of a strongly basic hydroxide, $(C_6H_5)_2I \cdot OH$, **diphenyliodonium hydroxide**, which has only been prepared in the form of its salts; it is an interesting fact that such derivatives of tervalent iodine should show basic properties.

These remarkable compounds were discovered and investigated by

Willgerodt and by V. Meyer; analogous compounds may be prepared from other iodo-derivatives containing the iodine atom directly united with the benzene (or a benzenoid) nucleus, but the dichlorides of aliphatic iodides, such as $C_2H_5 \cdot ICl_2$, only exist at low temperatures.

Chlorotoluene, $C_6H_4Cl \cdot CH_3$ (tolyl chloride), being a di-substitution product of benzene, exists in three isomeric modifications, only two of which—namely, the *o*- and *p*-compounds—are formed when *cold* toluene is treated with chlorine in the presence of iodine or iron; the three isomerides may be separately obtained, and are often prepared from the corresponding toluidines by Sandmeyer's method (p. 375),



o-Chlorotoluene boils at 159° , *m*-chlorotoluene at 162° , and *p*-chlorotoluene at 163° ; they resemble chlorobenzene in most respects, but, since they contain a methyl-group, they have also some of the properties of aliphatic compounds; on oxidation, they are converted into the corresponding *chlorobenzoic acids*, $C_6H_4Cl \cdot COOH$, just as toluene is transformed into benzoic acid.

The isomeric *bromotoluenes* are prepared by methods similar to those used in the case of the chloro-compounds; the *iodotoluenes* are obtained by diazotising the toluidines and treating the diazonium salts with potassium iodide (p. 403).

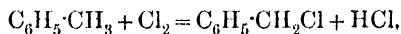
The boiling (and melting) points of these compounds are given below:

Bromotoluenes, *o*-, 182° ; *m*-, 184° ; *p*-, 185° (m.p. 28°).

Iodotoluenes, *o*-, 204° ; *m*-, 204° ; *p*-, 213° (m.p. 34°).

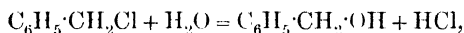
These data afford good examples of the general rule (p. 363) that the *p*-compounds have usually higher boiling-points than either the *o*- or the *m*-isomerides.

Benzyl chloride, $C_6H_5 \cdot CH_2Cl$, although isomeric with the three chlorotoluenes, differs from them very widely in many respects, and may be taken as an example of that class of halogen compounds in which the halogen is present in the *side-chain*. It may be obtained by treating benzyl alcohol (p. 435) with hydrogen chloride, but is always prepared by passing chlorine into *boiling* toluene,



The toluene is contained in a flask which is heated on a sand-bath and connected with a reflux condenser; a stream of dry chlorine is then passed into the boiling liquid, until the theoretical gain in weight has taken place, and the product is purified by fractional distillation; the action takes place most rapidly in strong sunlight.

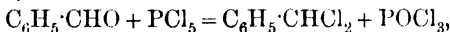
Benzyl chloride is a colourless, unpleasant-smelling liquid, boiling at 176° ; it is practically insoluble in water, but is miscible with most organic liquids. It behaves like other aromatic compounds towards nitric acid, by which it is converted into a mixture of isomeric nitro-compounds, $C_6H_5(NO_2) \cdot CH_2Cl$. At the same time, however, it has many properties in common with the alkyl halides; thus it is slowly decomposed by boiling water, yielding the corresponding hydroxy-compound, *benzyl alcohol* (p. 435),



and it reacts with alcoholic ammonia, potassium cyanide, silver acetate, and many other compounds, giving benzyl derivatives corresponding with those obtained from the alkyl halides.

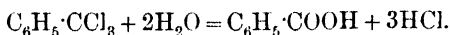
Benzyl chloride is a substance of considerable commercial importance, and is used for the preparation of benzyl alcohol (p. 436) and benzyl derivatives of aniline.

Benzal chloride or **benzylidene dichloride**,¹ $C_6H_5 \cdot CHCl_2$, may be obtained by treating benzaldehyde with phosphorus pentachloride,



but it is prepared on the large scale by chlorinating toluene, just as described in the case of benzyl chloride, except that the process is continued until twice as much chlorine has been absorbed. It boils at 213° , and is hydrolysed by water and by aqueous alkalis giving benzaldehyde (p. 438), for the preparation of which it is used.

Benzotrichloride, $C_6H_5 \cdot CCl_3$ (phenylchloroform), is also prepared by chlorinating boiling toluene; it boils at 213° , and when heated with water, it is converted into benzoic acid,



¹ The name *benzal* or *benzylidene* is given to the group of atoms, $C_6H_5 \cdot CH <$, which is analogous to ethylidene, $CH_3 \cdot CH <$.

It is interesting to note that those toluene derivatives in which the halogen is in the side-chain are lachrymatory (benzyl bromide was used in the war of 1914-18), whereas compounds such as the chlorotoluenes, with the halogen combined with carbon of the nucleus, have hardly any action on the eyes. The three side-chain halogen derivatives of toluene are all important because of their use in the large-scale preparation of benzyl alcohol, benzaldehyde and benzoic acid respectively.

Aromatic Grignard reagents.

Many aromatic halogen derivatives, like the alkyl halides, react readily with magnesium in the presence of pure ether, and the *Grignard reagents* which are thus formed show the reactions of those of the aliphatic series (p. 208).

Magnesium phenyl bromide, $C_6H_5 \cdot MgBr$, and **magnesium benzyl chloride**, $C_6H_5 \cdot CH_2 \cdot MgCl$, are common reagents of this type. They are decomposed by water, giving benzene and toluene respectively, so that the aromatic monohalogen derivatives may be easily transformed into the parent hydrocarbons.

The aromatic or *aryl* Grignard reagents, being easily prepared, have been very much used in the synthesis of secondary and tertiary aryl alcohols (p. 437), and of aryl derivatives of both metals and non-metals.

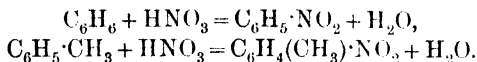
CHAPTER XXV.

NITRO-COMPOUNDS.

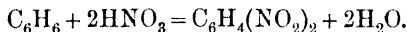
It has already been stated that one of the more characteristic properties of aromatic compounds is the readiness with which they may be converted into nitro-derivatives, by the substitution of nitro-groups for hydrogen of the *nucleus*; the compounds formed in this way are of the greatest importance, more especially because it is from them that the amino- and diazonium-compounds are prepared.

Preparation.—Many aromatic compounds are '*nitrated*'—that is to say, converted into their nitro-derivatives—when they are treated with concentrated nitric acid (sp. gr. 1.3 to 1.5), in

the cold or at ordinary temperatures, and under such conditions a mononitro-compound is usually produced ; benzene, for example, yields *nitrobenzene*, and toluene, a mixture of *o*- and *p*-*nitrotoluenes*,



Some aromatic compounds, however, are only very slowly acted on by nitric acid alone ; in such cases a mixture of concentrated nitric and sulphuric acids is used. This mixture is also employed in many cases, even when nitric acid alone might be used, because nitration then takes place more readily. When a large excess of such a mixture is used, and especially when heat is applied, the aromatic compound may be converted into (a mixture of isomeric) dinitro- or trinitro-derivatives ; benzene, for instance, yields a mixture of three *dinitrobenzenes*, the principal product, however, being the meta-compound,



In carrying out nitrations the aromatic compound is added to the acid or *vice versa* in *small* quantities at a time, otherwise the reaction may be too violent ; in all such experiments particular precautions must be taken to avoid accidents.

Generally speaking, the number of hydrogen atoms displaced by nitro-groups is the larger the higher the temperature and the more concentrated the acid, or mixture of acids, employed, but depends to an even greater extent on the nature of the substance undergoing nitration ; as a rule, the introduction of nitro-groups is facilitated when other atoms or groups, especially hydroxy- or alkyl-groups, have already been substituted for hydrogen of the nucleus. The *nature* of these atoms or groups, moreover, determines the position taken up by the entering nitro-group ; if the substituent group is $-\text{NO}_2$, $-\text{COOH}$, or $-\text{SO}_3\text{H}$, the *m*-nitro-derivative is formed, whereas, when the atom or group in question is a halogen, or an alkyl-, amino-, or hydroxyl-group, a mixture of the *o*- and *p*-nitro-derivatives is produced.

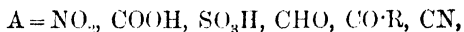
This *directing* or *orientating* influence of an atom or group, already combined with the nucleus, on the position which is taken up by a second substituent, is not restricted to the case of a nitro-group, but is observed in the formation of *all* benzene substitution products, except, of course, in that of the mono-

derivatives ; so regularly, in fact, is this influence exercised that it is possible to summarise the course of those reactions, which give di-substitution products, in the following statements :

The relative position taken up by one of the following atoms or groups, Cl, Br, NO_2 , SO_3H , which are capable of *directly* displacing hydrogen of the nucleus, depends on the nature of the atom or group, A, already united with the nucleus.

When $\text{A} = \text{Cl}, \text{Br}, \text{I}, \text{NH}_2, \text{NHR}, \text{NR}_2, \text{OH}, \text{CH}_3$ (or other alkyl-group), the product consists almost entirely of a mixture of the *para*- and the *ortho*-compounds.¹

When, on the other hand,



a *meta*-derivative is the principal product, and relatively very small quantities of the *ortho*- and *para*-compounds are formed.

This general behaviour may also be summarised as follows (*Crum Brown's rule*) : When the atom or group, A, in a mono-substitution product is such that its hydrogen compound, HA, cannot be *directly* oxidised to $\text{HO}\cdot\text{A}$, the di-substitution product is a mixture of the *ortho*- and *para*-compounds ; if, on the other hand, HA can be directly oxidised to $\text{HO}\cdot\text{A}$, the product is the *meta*-compound.

An alternative rule is : when an atom, A, united to the nucleus, is combined to a *different* element by a double or semi-polar bond, *meta*-substitution occurs ; otherwise, *ortho*- and *para*-derivatives are formed.

These statements also hold good when two identical atoms or groups are introduced in one operation, since the change really takes place in *two stages* ; when benzene, for example, is treated with nitric acid, *meta*-dinitrobenzene is the principal product, whereas bromine gives mainly *para*-dibromobenzene. It is very important to remember this *orientating* effect of particular atoms and groups and to understand that *meta*-nitrochlorobenzene, for example, may be obtained by chlorinating nitrobenzene, but *not* by nitrating chlorobenzene.

Properties.—Certain aromatic nitro-compounds have a more or less intense yellow colour ; as they are usually crystalline they often serve for the identification of hydrocarbons and other liquids. Many of them are volatile in steam, but, with the exception of certain mononitro-derivatives, they cannot be distilled under

¹ In Friedel and Crafts' reaction toluene gives *m*-xylene as the main product (p. 366), but as a rule the *orientating* effect of the CH_3 - group is as stated.

atmospheric pressure, because when heated strongly they decompose, sometimes with explosive violence; an explosion may also occur when they are heated with sodium, in testing for nitrogen. They are generally sparingly soluble in water, but readily soluble in benzene, ether, alcohol, &c. As in the case of the nitro-paraffins (p. 175), the nitro-group is very firmly combined, and, as a rule, is not displaced by the hydroxyl-group even when the compound is heated with aqueous or alcoholic potash.

The most important reaction of the nitro-compounds—viz. their behaviour on reduction—is described later (p. 386).

Nitrobenzene, $C_6H_5NO_2$, is usually prepared in the laboratory by slowly adding to benzene (10 parts)¹ a mixture of nitric acid of sp. gr. 1·45 (12 parts), and concentrated sulphuric acid (16 parts), the temperature being kept below about 40°.

The benzene is placed in a flask (which must *not* be corked), and the acid mixture is *slowly* added from a dropping funnel. The flask is cooled in water and is given a rotatory motion during the operation. As soon as all the acid has been added, the product is heated at about 80° during half an hour, then cooled, and poured into 5–10 volumes of water; the nitrobenzene is separated with the aid of a tap funnel, washed with a little dilute alkali until free from acid, and well shaken with a few small lumps of anhydrous calcium chloride; as these dissolve, more are added, and so on, until the nitrobenzene becomes clear. It is then filtered into a distillation flask and fractionated (if incompletely dried, the contents of the flask crackle and splutter when heat is applied); the liquid collected from about 200–215° is sufficiently free from impurity for ordinary purposes, and any dinitrobenzene which may have been formed will be obtained as a residue.

On the large scale, nitrobenzene is prepared in a similar manner, but the operation is carried out in iron vessels provided with stirrers; the product is separated from the acid mixture and exposed to a current of steam until free from benzene.

Nitrobenzene is a pale-yellow oil of sp. gr. 1·2 at 20°, and has a strong smell, which is very like that of benzaldehyde (p. 439); it boils at 209°, is volatile in steam, and is miscible with organic liquids, but is practically insoluble in water. In spite of the fact that it is poisonous, it was formerly employed, instead of oil of bitter almonds, for flavouring and perfuming purposes, under the name of 'essence of myrbane'; its principal use, however, is for the manufacture of aniline (p. 390).

¹ Compare footnote, p. 361.

Meta-dinitrobenzene, $C_6H_4(NO_2)_2$, is obtained, together with small quantities of the *o*- and *p*-dinitro-compounds, by the nitration of nitrobenzene (or of benzene).

Nitrobenzene (1 part) is gradually run into a mixture of nitric acid (sp. gr. 1.5; $1\frac{1}{2}$ parts) and concentrated sulphuric acid ($1\frac{1}{2}$ parts) to which a few small pieces of unglazed earthenware have been added; the flask is then heated on a sand-bath, until a drop of the oil solidifies completely when it is stirred with cold water. When cold, the mixture is poured into a large volume of water, and the solid is separated by filtration, washed with water, and recrystallised from hot alcohol until its melting-point is constant; the *o*- and *p* compounds, which together form only about 8 per cent. of the original product, remain in the mother-liquors.

m-Dinitrobenzene crystallises in pale-yellow needles, melts at 90° , and is volatile in steam; it is only very sparingly soluble in boiling water and is very poisonous. On reduction with alcoholic ammonium sulphide (p. 387), it is first converted into **m-nitroaniline** (p. 394), and then into **m-phenylenediamine** (**m-diaminobenzene**), $C_6H_4(NH_2)_2$ (p. 395).

o-Dinitrobenzene and **p-dinitrobenzene** are colourless and melt at 118° and 173° respectively; the former may be obtained from the mother-liquor from the crystallisation of the crude **m**-compound (see above) and the latter by oxidising quinone dioxime (p. 446) with nitric acid. They resemble the corresponding **m**-compound in their behaviour on reduction, and in most other respects. **o-Dinitrobenzene**, however, differs notably from the other two isomerides, inasmuch as with boiling caustic soda, it yields **o-nitrophenol** (p. 426), and with alcoholic ammonia, at moderately high temperatures, it gives **o-nitroaniline** (p. 394). A similar behaviour is observed in the case of other *o*-dinitro-compounds, the presence of the one nitro-group rendering the other more easily displaceable.

Symmetrical **trinitrobenzene**, $C_6H_3(NO_2)_3$, is formed when the **m**-dinitro-compound is heated with a mixture of nitric and anhydrosulphuric acids; it is colourless, and melts at $121-122^\circ$.

The halogen derivatives of benzene are readily nitrated, yielding, however, the *o*- and *p*-mononitro-derivatives only, according to the orientation rule (p. 382); the **m**-nitro-halogen compounds, therefore, are prepared by chlorinating or brominating nitrobenzene. All these nitro-halogen derivatives are crystalline, and, as will be seen from the following table, their melting-points

exhibit the regularity already mentioned (p. 363) except in the case of *m*-iodonitrobenzene :

		Ortho.	Meta.	Para.
Chloronitrobenzene,	$C_6H_4Cl \cdot NO_2$,	32.5°	44°	83°
Bromonitrobenzene,	$C_6H_4Br \cdot NO_2$,	43	56	126
Iodonitrobenzene,	$C_6H_4I \cdot NO_2$,	52	36	174

They are, on the whole, very similar in chemical properties, except that, as already pointed out (p. 375), the *o*- and *p*-compounds differ from the *m*-compounds in their behaviour with alcoholic potash and ammonia, a difference which recalls that shown by the three dinitrobenzenes.

The **nitrotoluenes**, $C_6H_4(CH_3) \cdot NO_2$, are important, because they serve for the preparation of the toluidines (p. 394). The *o*- and *p*-compounds are prepared by nitrating toluene, and may be separated by fractional distillation under reduced pressure, combined with crystallisation at low temperatures; *o*-nitrotoluene melts at -4° , and boils at 222° , whereas *p*-nitrotoluene melts at 51° , and boils at 238° . *m*-Nitrotoluene is also formed in very small proportions by nitrating toluene; it melts at 16° , and boils at 230° .

Trinitrotoluene, $C_6H_2(CH_3)(NO_2)_3$ [$3NO_2 = 2:4:6$],¹ manufactured by the further nitration of the mixture of *o*- and *p*-nitrotoluenes, is a very important explosive (T.N.T.); it melts at 82° without decomposing, but it can be detonated with mercury fulminate (p. 319); mixed with ammonium nitrate, it forms the explosive, *amatol*.

On oxidation with dichromate and sulphuric acid, trinitrotoluene gives *trinitrobenzoic acid*, which loses carbon dioxide when it is heated with water; the product, on reduction, yields triaminobenzene, which is converted into phloroglucinol (p. 433) by boiling hydrochloric acid.

Phenylnitromethane, $C_6H_5 \cdot CH_2 \cdot NO_2$, is an example of a compound which contains a nitro-group in the side-chain. It is obtained by the interaction of *benzyl iodide*, $C_6H_5 \cdot CH_2I$, and silver nitrite, and is a colourless liquid, boiling at 141° (35 mm.). Like the primary and secondary nitroparaffins, it is a *pseudo-acid* (p. 177), and gives, with sodium hydroxide, a salt, $C_6H_5 \cdot CH \cdot NO \cdot ONa$, which is derived from the acid, $C_6H_5 \cdot CH \cdot NO \cdot OH$; this acid is obtained as a crystalline precipitate (m.p. 84°) when the sodium salt is treated with a mineral acid in aqueous solution, but it soon undergoes isomeric change into phenylnitromethane, even at ordinary temperatures.

¹ When, as in this case, one of the substituents (namely the CH_3 - group) is not shown in the brackets, it must be taken to be in the 1-position.

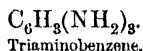
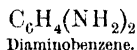
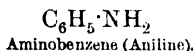
CHAPTER XXVI.

AMINO-COMPOUNDS AND AMINES.

THE hydrogen atoms in aromatic compounds may be indirectly displaced by amino-groups, and in this way bases, such as *aniline*, $C_6H_5 \cdot NH_2$, *benzylamine*, $C_6H_5 \cdot CH_2 \cdot NH_2$, and *diaminobenzene*, $C_6H_4(NH_2)_2$, which are analogous to, and have many properties in common with, the aliphatic amines, are produced; as, however, those compounds, which contain the amino-group directly united with carbon of the nucleus, differ in several respects from those in which this radical is present in the side-chain, and, moreover, are of much greater importance than the latter, they may be considered as forming a separate group, the members of which will be referred to as *amino-compounds*.

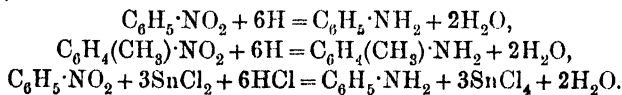
Amino-Compounds.

The amino-compounds, therefore, are derived from benzene and other aromatic substances, by the substitution of one or more amino-groups for hydrogen atoms of the *nucleus*; they may be classed as mono-, di-, tri-, &c., amino-compounds, according to the number of such groups which they contain,



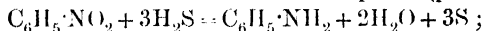
With the exception of aniline, the homologous amino-compounds show the usual isomerism; there are, for example, three isomeric (*o.m.p.*) *diaminobenzenes*, and three isomeric (*o.m.p.*) *aminotoluenes*, or *toluidines*, $C_6H_4(CH_3) \cdot NH_2$, a fourth isomeride of the toluidines—namely, *benzylamine*, $C_6H_5 \cdot CH_2 \cdot NH_2$ (p. 399)—being also known.

Preparation.—The amino-compounds are nearly always prepared by the reduction of the nitro-compounds; various reducing agents, such as tin, zinc, or iron, with hydrochloric or acetic acid, are employed, and also a solution of stannous chloride in hydrochloric acid,



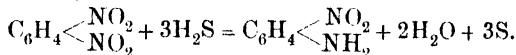
Reduction is usually effected by merely treating the nitro-compound with the reducing agent, when a vigorous reaction often ensues, and the application of heat is seldom necessary except towards the end of the operation. The solution then contains the amino-compound, combined as a simple salt; when, however, tin, or stannous chloride, and hydrochloric acid have been used, a complex salt, $B_{20}H_2SnCl_6$, may be produced from the hydrochloride of the base and the stannic chloride which has been formed. In either case the amino-compound is liberated by adding excess of caustic soda (or lime), and is distilled in steam or extracted with ether or some other solvent; when tin and hydrochloric acid, or stannous chloride, has been used, the acid solution may be treated with hydrogen sulphide, filtered, and evaporated, in order to obtain the hydrochloride of the amino compound.

Nitro-compounds may also be reduced to amino-compounds in *alkaline* solution with hydrogen sulphide, or, more conveniently, with an alcoholic solution of ammonium sulphide (p. 394),



a mixture of ferrous sulphate and an alkali hydroxide in aqueous solution is also frequently employed.

When a compound contains two or more nitro-groups it may be partially reduced by treating its alcoholic solution either with the calculated quantity of stannous (or titanous) chloride and hydrochloric acid, or with ammonia and hydrogen sulphide; in the latter, as in the former case, one nitro-group is reduced before a second is attacked, so that if the current of gas is stopped at the right time (which must be ascertained by experiment), partial reduction only takes place. Dinitrobenzene, for example, can be converted into nitroaniline by either of these methods, the latter being the more convenient,



Amino-compounds may also be obtained by reducing certain nitroso-derivatives (p. 397) and also azo- and hydrazo-compounds (p. 412).

The monoamino-derivatives of benzene, toluene, xylene, &c. are prepared commercially in large quantities by reducing the nitro-compounds with iron and hydrochloric acid.

The diamino-compounds, such as the *o*-, *m*-, and *p*-diamino-benzenes or phenylenediamines, $C_6H_4(NH_2)_2$, are prepared by reducing either the corresponding *dinitrobenzenes*, $C_6H_4(NO_2)_2$, or the *nitroanilines*, $C_6H_4(NO_2) \cdot NH_2$.

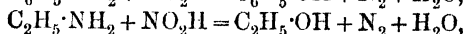
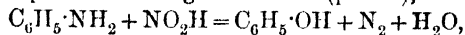
Properties.—The *monoamino*-compounds are mostly colourless liquids, which distil without decomposing, and are specifically heavier than water; they have a faint but characteristic odour, and dissolve freely in organic solvents, but are only sparingly soluble in water; on exposure to air and light they darken, and ultimately become brown or black.

They are comparatively weak bases, and are *neutral* to litmus, in which respect they differ from the strongly basic aliphatic amines and from the aromatic amines, such as benzylamine (p. 399), which contain the amino-group in the *side-chain*; for this and other reasons (p. 424), the phenyl-group may be regarded as a negative or acidic radical. Nevertheless, the amino-compounds combine with acids to form salts, such as *aniline hydrochloride*, $C_6H_5 \cdot NH_2 \cdot HCl$, and *phenylenediamine dihydrochloride*, $C_6H_4(NH_2)_2 \cdot 2HCl$.¹ The simple salts of the amino-compounds are usually soluble in water, by which they are hydrolysed to a greater or less extent; they are completely decomposed by an excess of caustic alkali or alkali carbonate.

When two hydrogen atoms in ammonia are displaced by phenyl-groups, as in *diphenylamine*, $(C_6H_5)_2NH$ (p. 398), the product is so feebly basic that its salts are almost completely hydrolysed by water. *Triphenylamine*, $(C_6H_5)_3N$ (p. 398), moreover, does not form salts at all.

For a similar reason, the hydroxy-, nitro-, and halogen-derivatives of the amino-compounds, such as *aminophenol*, $C_6H_4(OH) \cdot NH_2$, *nitroaniline*, $C_6H_4(NO_2) \cdot NH_2$, *chloroaniline*, $C_6H_4Cl \cdot NH_2$, &c., are also weaker bases than the amino-compounds themselves, because the presence of the negative group or atom, $HO-$, NO_2- , $Cl-$, &c., enhances the acidic character of the phenyl radical.

The amino-compounds *differ* from the aliphatic primary amines, and from those aromatic primary amines which contain the amino-group in the *side-chain*, in their characteristic behaviour towards nitrous acid. Although, when their salts are *warmed* with nitrous acid (a nitrite and an acid) in aqueous solution, they yield phenols by the substitution of the hydroxy- for the amino-group, just as the aliphatic amines give alcohols (p. 194),

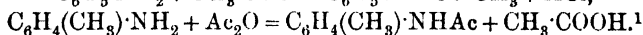
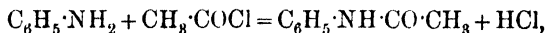


¹ These formulæ may also be written $[C_6H_5 \cdot NH_2]Cl$ and $[C_6H_4(NH_2)_2]Cl_2$ respectively (p. 211).

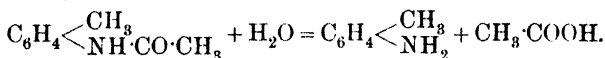
in the *cold* (usually at about 0°), under otherwise the same conditions, they are converted into *diazonium-salts* (p. 400), substances which are not produced from the primary aliphatic amines.

It will be evident from the above statements that there are several important differences between the amino-compounds and the aliphatic primary amines, the character of an amino group of the nucleus being influenced by its state of combination; nevertheless, except as regards those points already mentioned, amino-compounds have, on the whole, properties very similar to those of the aliphatic primary amines. The amino-compounds, like the latter, react readily with alkyl halides, yielding mono- and dialkyl derivatives, such as *methylaniline*, $C_6H_5 \cdot NH \cdot CH_3$, *dimethylaniline*, $C_6H_5 \cdot N(CH_3)_2$, &c., and also quaternary ammonium salts (p. 197), such as *phenyltrimethylammonium iodide*, $C_6H_5 \cdot N(CH_3)_3 I$, or $[C_6H_5 \cdot N(CH_3)_3]I$ (p. 211).

They are also readily changed by acid chlorides and anhydrides, yielding substances such as *acetanilide* and *acetotoluide*, which are closely allied to, and may be regarded as derived from, the aliphatic amides,

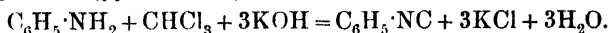


These *substituted amides* are crystalline, and serve for the identification of the (liquid) amino-compounds; like the amides, they are hydrolysed by boiling acids or alkalis,



Boiling sulphuric acid, previously diluted with about an equal volume of water, is generally the most suitable reagent, but many hours may be necessary to complete the hydrolysis.

The amino-compounds, like the aliphatic primary amines, give the carbylamine reaction; when a trace of aniline, for example, is heated with alcoholic potash and chloroform, an intensely nauseous smell is observed, due to the formation of phenyl-carbylamine (pp. 195, 317),



Diamino- and *triamino-compounds*, such as the three (*o.m.p.*) *phenylenediamines* or *diaminobenzenes*, $C_6H_4(NH_2)_2$, and the

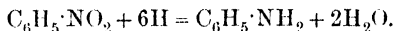
¹ Ac represents the *acyl* radical (acetyl group), $-CO \cdot CH_3$.

triaminobenzenes, $C_6H_3(NH_2)_3$, are very similar to the monoamino-compounds in chemical properties, but differ from them usually in being solid, more readily soluble in water, and less volatile; the triamino-compounds generally form salts, such as $C_6H_3(NH_2)_3 \cdot 2HCl$, with only *two* equivalents of an acid.

Aniline and its Derivatives.

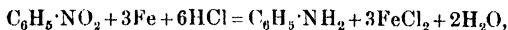
Aniline, $C_6H_5 \cdot NH_2$ (aminobenzene, phenylamine), was first obtained by Unverdorben in 1826 by strongly heating indigo.¹ Runge in 1834 showed that aniline is contained in small quantities in coal-tar; its preparation from nitrobenzene was first accomplished by Zinin in 1841.

Aniline may be prepared by the reduction of nitrobenzene with iron and hydrochloric acid, a method which is used on a very large scale,

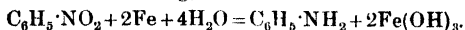


Nitrobenzene (25 grams) and iron borings (43 grams) are heated together on a water-bath in a 250 c.c. flask, fitted with a short, wide air-condenser, and concentrated hydrochloric acid (15 c.c.) is added through the condenser in *small* quantities at a time in the course of about 20 minutes, after which heating is continued during about 15 minutes longer. The contents of the flask are *vigorously* shaken from time to time, especially after each addition of the acid. A concentrated solution of sodium hydroxide (about 5 g.) is then slowly added, and the liberated aniline is distilled in steam. The distillate is saturated with salt, and the base is separated, dried over solid potash, decanted into a dry flask, and purified by distillation.

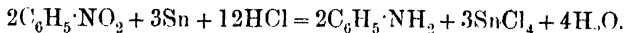
The quantity of hydrochloric acid used on the large scale is about $\frac{1}{6}$ th of that calculated from the equation,



because in the presence of ferrous chloride, aniline is formed by other reactions, such as the following,



In preparing aniline in the laboratory, tin and hydrochloric acid may also be employed,



The operation is carried out with the apparatus just described, using nitrobenzene (25 g.), granulated tin (45 g.), and concentrated hydrochloric acid (90 c.c.), which is added in *small* portions at a time. The mixture is

¹ The name aniline is derived from *an-nîl* (*al-nîl*), the Arabic for the indigo plant.

not heated, and must be cooled if the reaction becomes too violent. When all the acid has been added, the flask is left on a water-bath until drops of oil are no longer visible, and is then cooled until the product, *aniline stannichloride* (p. 387) begins to crystallise; a cold solution of sodium hydroxide (45 g.) in water (about 100 c.c.) is added *very cautiously*, in small quantities at a time, the flask being well shaken, and the liberated aniline is isolated, as described above.

Aniline is a *poisonous* oil, boiling at 184° , and having a faint odour, which is common to many amino-compounds; it is sparingly soluble in water, and ordinary samples turn yellow when exposed to light and air, becoming ultimately almost black. Although neutral to litmus, aniline has very decided basic properties, and, with acids, it forms soluble salts, such as aniline *hydrochloride*, $C_6H_5 \cdot NH_2 \cdot HCl$, and the rather sparingly soluble normal *sulphate*, $(C_6H_5 \cdot NH_2)_2 \cdot H_2SO_4$. The former, like the hydrochlorides of the aliphatic amines, forms complex salts with platinic and auric chlorides; a moderately concentrated solution of the hydrochloride gives with platinic chloride, for example, the *platinichloride*, $(C_6H_5 \cdot NH_2)_2 \cdot H_2PtCl_6$, which is precipitated in yellow plates, and is only moderately soluble in water.

When one drop of aniline is heated with chloroform and alcoholic potash, it yields phenylcarbylamine, a substance readily recognised by its extremely disagreeable odour; aniline may also be detected by treating its aqueous solution with bleaching-powder or sodium hypochlorite, when an intense purple colouration is produced.

These qualitative reactions, combined with a determination of the boiling-point, are sufficient for the identification of aniline; if in the form of a salt, and the boiling-point of the base is not known, aniline may be identified with the aid of its *acetyl-* or *benzoyl-*derivative (*benzanilide*), or its *tribromo-*derivative (p. 393).

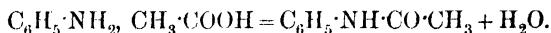
When acid solutions of the salts of aniline are treated with nitrous acid in the cold, diazonium-salts (p. 400) are formed, but at higher temperatures, the latter are decomposed, with formation of phenol (p. 425).

Aniline is very largely employed in the manufacture of dyes, and in the preparation of a great many other benzene derivatives which are described later.

Acetanilide, $C_6H_5 \cdot NH \cdot CO \cdot CH_3$, is formed when aniline is treated with acetyl chloride or acetic anhydride.

The product of the (vigorous) reaction is treated with cold water, in order to extract the aniline hydrochloride or acetate, which is also formed, and the undissolved acetanilide is then recrystallised from boiling water.

It is conveniently prepared by boiling aniline (10g.) with glacial acetic acid (15 g.) on a reflux apparatus during 2-4 hours, when the aniline acetate which is first formed is slowly converted into acetanilide, with elimination of water,

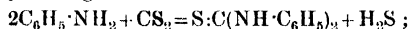


The conversion is not complete, because the reaction is reversible, but the acetanilide is easily separated from unchanged aniline acetate and purified, in the manner just described.

Acetanilide crystallises in plates, melts at 114° , and is very sparingly soluble in cold, but readily so in hot, water; when heated with acids or alkalis, it is hydrolysed, giving aniline and acetic acid. It is used in medicine, under the name of *antifebrin* or *acetanilidum*, for reducing the body-temperature in cases of fever.

Formanilide, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{CHO}$ (m.p. 40°), the anilide of formic acid, and *oxanilide*, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{CO}\cdot\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_5$ (m.p. 245°), the anilide of oxalic acid, may be prepared by heating the corresponding aniline salts; *benzanilide*, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{CO}\cdot\text{C}_6\text{H}_5$ (m.p. 163°), is easily prepared by the Schotten-Baumann method (p. 453).

Thiocarbanilide, $\text{S}:\text{C}(\text{NH}\cdot\text{C}_6\text{H}_5)_2$, or *diphenylthiourea*, is prepared by passing the vapour of carbon disulphide into aniline, which is heated at about 100° , or by boiling a mixture of the two substances,

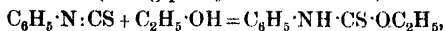


it crystallises in colourless plates, melting at 151° , and is used to hasten the vulcanisation of rubber. When it is boiled with concentrated hydrochloric acid, it first yields *phenyl isothiocyanate* (*phenyl mustard oil*) and *aniline*,

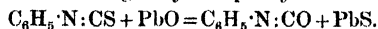


and then *triphenylguanidine*, $\text{C}_6\text{H}_5\text{N}:\text{C}(\text{NH}\cdot\text{C}_6\text{H}_5)_2$ (m.p. 143°), and other products.

Phenyl isothiocyanate, $\text{C}_6\text{H}_5\cdot\text{N}:\text{CS}$, obtained as described above, is a colourless liquid (b.p. 222°), with a characteristic disagreeable smell. It reacts with alcohols giving phenyl thiourethanes,

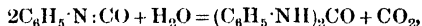


and when heated with litharge it yields *phenyl carbimide*,

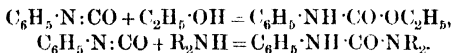


Phenyl carbimide, $\text{C}_6\text{H}_5\cdot\text{N}:\text{CO}$, usually prepared by heating aniline hydrochloride at about 200° , in a stream of carbonyl chloride, is an unpleasant

smelling liquid, boiling at 166°. It is slowly decomposed by water, giving *diphenylurea*,

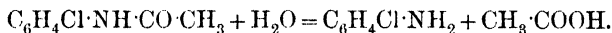


and is used for the characterisation of alcohols and amines (primary and secondary), with which it yields (crystalline) phenylurethanes and phenylurea derivatives respectively,



Halogen Substitution Products of Aniline.—Aniline and, in fact, most amino-compounds are much more readily attacked by halogens than are the hydrocarbons. When aniline, for example, is treated with an excess of chlorine- or bromine-water, it is at once converted into *trichloroaniline*, $\text{C}_6\text{H}_2\text{Cl}_3\cdot\text{NH}_2$ (m.p. 77°), or *tribromoaniline*, $\text{C}_6\text{H}_2\text{Br}_3\cdot\text{NH}_2$ (m.p. 119°); both of these compounds contain the halogen atoms in the 2:4:6-positions and their salts are completely hydrolysed by water.

The *o*- and *p*-chloroanilines, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{NH}_2$, may be prepared by passing chlorine into acetanilide, the *p*-derivative being obtained in the larger quantity. The two isomerides are first separated by crystallisation, and are then decomposed by boiling alkalis or acids,



The effect of introducing an acetyl radical into the amino-group, and thus protecting or *blocking* the latter, is to make the aniline less reactive; acetanilide, in fact, behaves towards halogens more like benzene than like aniline, but is more reactive than the former.

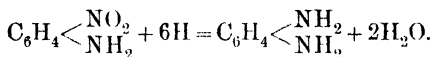
m-Chloroaniline is most conveniently prepared by the reduction of *m*-chloronitrobenzene, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{NO}_2$ (a substance which is formed by chlorinating nitrobenzene in the presence of antimony). *o*-Chloroaniline and *m*-chloroaniline boil at 207° and 230° respectively; *p*-chloroaniline melts at 70° and boils at 230°.

The *nitroanilines*, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{NH}_2$, cannot be prepared by nitrating aniline, because the base undergoes oxidation and other complex changes occur; when, however, the amino-group is 'protected' or 'blocked' by the introduction of an acetyl radical (see above), nitration takes place in a normal manner; the acetyl derivatives of *o*- and *p*-nitroaniline which are formed, are separated, and then converted into the corresponding nitroanilines by hydrolysis with diluted hydrochloric acid.

m-Nitroaniline is conveniently prepared by the partial reduction of **m**-dinitrobenzene with ammonium sulphide (p. 387).

m-Dinitrobenzene (2 parts), alcohol (6 parts), and strong ammonium hydroxide solution (1 part) are placed in a flask, and hydrogen sulphide is passed into the liquid, which, later on, is warmed from time to time. The dinitrobenzene gradually disappears and sulphur is deposited. The contents of the flask are tested at intervals, in order to ascertain when the stream of hydrogen sulphide should be stopped. For this purpose a small quantity of the solution and a portion of the deposit are evaporated together in a basin on the water-bath, and the residue is treated with cold dilute hydrochloric acid, which dissolves **m**-nitroaniline (in the form of its hydrochloride), but not dinitrobenzene or sulphur; the residue insoluble in dilute acid is then extracted with a little boiling alcohol, and the filtered solution is treated with water (or evaporated), in order to prove the presence or absence of **m** dinitrobenzene (sulphur is only very sparingly soluble in alcohol). When the test portion gives a satisfactory result, the **m**-nitroaniline is extracted from the whole of the product in the manner just described, the acid solution is treated with excess of caustic soda, and the precipitated base is purified by recrystallisation from boiling water or very dilute aqueous alcohol.

o-Nitroaniline melts at 71° , **m**- at 114° , and **p**- at 147° ; they are all sparingly soluble in cold water, readily in alcohol, and on reduction they yield the corresponding **o**-, **m**-, and **p**-phenylenediamines (p. 395),



Homologues of Aniline.—The **toluidines** or amino-toluenes, $\text{C}_6\text{H}_4(\text{CH}_3)\text{NH}_2$, may be prepared by reducing the corresponding **o**-, **m**-, and **p**-nitrotoluenes (p. 385), with iron or tin, and hydrochloric acid, as described in the case of the preparation of aniline from nitrobenzene; the **o**- and **p**-compounds may also be obtained from methylaniline (p. 396). Both **o**- and **m** toluidine are oils, boiling at 199° and 203° respectively, but **p**-toluidine is crystalline, and melts at 45° , boiling at 200° .

The **o**-, **m**-, and **p**-acetotoluides, $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{CO}\cdot\text{CH}_3$, melt at 110° , 65° , and 145° respectively, the corresponding *benzotoluides*, $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{CO}\cdot\text{C}_6\text{H}_5$, at 131° , 125° , and 158° respectively. These compounds may serve for the identification of the bases (compare p. 452).

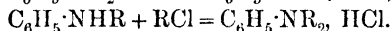
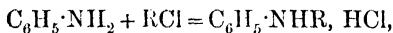
When treated with nitrous acid, the toluidines yield diazonium-salts, from which the corresponding cresols, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{OH}$, may be obtained (p. 385), and in all other reactions they show the greatest

similarity to aniline; *o*- and *p*-toluidine are employed in the manufacture of dyes.

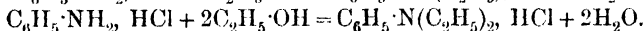
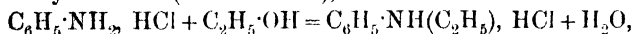
The **Diaminobenzenes** or *phenylenediamines*, $C_6H_4(NH_2)_2$, are obtained by the reduction of the corresponding dinitrobenzenes, or the nitroanilines, and a general description of their properties has been given (p. 389); commercial preparations often undergo atmospheric oxidation and turn brown. *o*-Phenylenediamine melts at 102° , the *m*- and *p*-compounds at 63° and 147° respectively. *m*-Phenylenediamine gives an intense yellow colouration with a trace of nitrous acid, and is employed in water-analysis for the detection and estimation of nitrites; both the *m*- and *p*-compounds are employed in the manufacture of dyes.

Alkylanilines.

Those derivatives of the amino-compounds, obtained by displacing one or both of the hydrogen atoms of the amino-group by alkyl radicals, are substances of considerable importance, and are usually known as **alkylanilines**. They are obtained by treating the amino-compounds with the alkyl halides, the reactions being analogous to those which occur in the formation of secondary, and tertiary, from primary, aliphatic amines (p. 196),



Instead of an alkyl halide, a mixture of an alcohol and an acid may be used, provided that a high temperature is employed; *methyl*- and *dimethyl aniline*, for example, are prepared, on the large scale, by heating aniline with methyl alcohol and a little sulphuric acid at about 230° under pressure, whereas *ethyl*- and *diethyl-aniline* are manufactured in a similar manner, using hydrochloric acid and ethyl alcohol (1 or 2 mols.),



In these reactions the alcohol is first converted into an alkyl hydrogen sulphate, or an alkyl halide, which then reacts with the base.

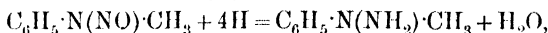
Since methyl- and dimethyl-aniline cannot be separated by fractional distillation, the latter is prepared as described above, using an excess of methyl alcohol, whereas the former is more conveniently obtained by running aniline and formalin separately into a vessel containing warm caustic soda and zinc dust; condensation occurs giving complex compounds, $[-CH_2 \cdot N(C_6H_5)-]_n$, which are then reduced mainly to methylaniline.

These mono- and di-alkyl derivatives are somewhat stronger bases than the amino-compounds from which they are formed, and are, in fact, similar in many important respects to the secondary and tertiary aliphatic amines respectively; they may be regarded as derived from the primary and secondary aliphatic amines respectively, by the substitution of a phenyl-group for a hydrogen atom, just as the secondary and tertiary aliphatic amines are obtained by the displacement of hydrogen atoms by alkyl-groups. Methylaniline, for example, is also *phenylmethylaniline*, and its properties are those of an aryl-substitution product of methylamine.

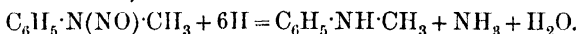
The mono-alkylanilines, like secondary aliphatic amines, are converted into pale-yellow *nitroso-amines* on treatment with nitrous acid,



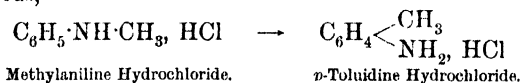
These nitroso-amines give Liebermann's nitroso-reaction (pp. 196, 424), and on reduction they yield a hydrazine derivative,



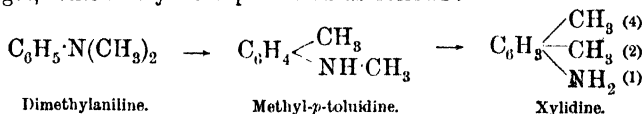
or are decomposed into ammonia and the alkylanilines from which they were derived,



When the hydrochloride of an alkylaniline, such as *methylaniline* or *dimethylaniline*, is heated at 280–300°, the alkyl-group leaves the nitrogen atom and displaces hydrogen from the nucleus,



In the case of dimethylaniline the change takes place in two stages, which may be represented as follows:



In the first *isomeric change*, the alkyl-group displaces hydrogen from the *para*-, and also from the *ortho*-position to the amino-group, but principally the former.

Methylaniline, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{CH}_3$, prepared as described above, is a colourless liquid, which boils at 194°, and has more strongly

marked basic properties than aniline. On the addition of sodium nitrite to its solution in excess of hydrochloric acid, *methylphenyl-nitrosoamine*, $\text{C}_6\text{H}_5\cdot\text{N}(\text{NO})\cdot\text{CH}_3$, is formed, and as this compound is *non-basic* it separates, as a light-yellow oil.

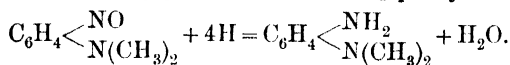
Methylacetanilide, $\text{C}_6\text{H}_5\cdot\text{N}(\text{CH}_3)\cdot\text{CO}\cdot\text{CH}_3$ (the acetyl derivative of methylaniline), melts at 102° , and *methylbenzanilide* or *benzoylmethylaniline*, $\text{C}_6\text{H}_5\cdot\text{N}(\text{CH}_3)\cdot\text{CO}\cdot\text{C}_6\text{H}_5$, at 63° .

Ethylaniline, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{C}_2\text{H}_5$, boils at 206° .

Dimethylaniline, $\text{C}_6\text{H}_5\cdot\text{N}(\text{CH}_3)_2$, the preparation of which has been given above, is a colourless, strongly basic oil, which boils at 192° ; it is largely used in the manufacture of dyes.

Diethylaniline, $\text{C}_6\text{H}_5\cdot\text{N}(\text{C}_2\text{H}_5)_2$, boils at 216° .

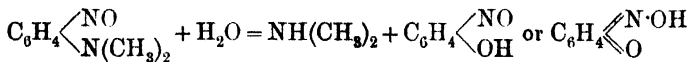
The *di-alkylanilines*, such as dimethylaniline, $\text{C}_6\text{H}_5\cdot\text{N}(\text{CH}_3)_2$, react very readily with nitrous acid (a behaviour which is *not* shown by tertiary aliphatic amines), intensely green nitroso-compounds (*not nitrosoamines*) being formed, the $-\text{NO}$ group displacing hydrogen of the *nucleus* from the *p*-position to the nitrogen atom. These substances do *not* give Liebermann's nitroso-reaction, and when reduced they yield derivatives of *p*-phenylenediamine,



***p*-Nitrosodimethylaniline**, $\text{C}_6\text{H}_4\begin{smallmatrix} \text{NO} \\ \text{N}(\text{CH}_3)_2 \end{smallmatrix}$, is prepared by treating dimethylaniline hydrochloride with nitrous acid.

Dimethylaniline (1 part) is dissolved in water (5 parts) and concentrated hydrochloric acid (2.5 parts), and to the *well-cooled* solution the theoretical quantity of sodium nitrite, dissolved in a little water, is slowly added. The yellow crystalline precipitate of *nitrosodimethylaniline hydrochloride* is separated by filtration, dissolved in water, and decomposed with sodium carbonate; the free base is extracted with, and crystallised from, ether.

It crystallises from ether in dark-green plates, melts at 85° , and is used for the manufacture of various dyes. When reduced with zinc and hydrochloric acid it is converted into *dimethyl-p-phenylenediamine* (see above), and when boiled with caustic soda it is decomposed into dimethylamine and *p-nitrosophenol* or *quinone monoxime* (compare p. 446),



The latter reaction, which is shown by the nitroso-compounds of all tertiary aromatic amines, is useful for the preparation of secondary aliphatic amines (compare p. 212), especially diethylamine.

Tetryl, $C_6H_2(NO_2)_3 \cdot N(CH_3) \cdot NO_2$, is a tetranitro-derivative of mono-methylaniline, produced by the energetic nitration of dimethylaniline. It is insoluble in water, melts at 127° , and is used as a detonating agent; with boiling alkalis it gives methylamine and picric acid (p. 427). *Tetranitroaniline*, $C_6H(NO_2)_4 \cdot NH_2$ [$4NO_2 = 2:3:4:6$], prepared from *m*-nitroaniline in a similar manner, is also used as an explosive and in detonators.

Diphenylamine and Triphenylamine.

The hydrogen atoms of the amino-group in aniline may also be displaced by phenyl radicals, the compounds *diphenylamine*, $(C_6H_5)_2NH$, and *triphenylamine*, $(C_6H_5)_3N$, being produced.

These substances can be obtained by heating aniline with bromo- or iodo-benzene, but only if some catalyst (copper or bronze) is employed.

Diphenylamine, $(C_6H_5)_2NH$, is prepared commercially by heating aniline hydrochloride with aniline at about 200° , in closed vessels,



It is crystalline, melts at 54° , boils at 302° , and is practically insoluble in water. It is only a feeble base, and its salts are decomposed by water; hence diphenylamine, unlike the great majority of bases, is not readily soluble in dilute mineral acids. Its solution in concentrated sulphuric acid gives, with a trace of nitric acid, an intense blue colouration, and, therefore, serves as a very delicate test for nitric acid or nitrates. Diphenylamine is used in the manufacture of dyes; also for experiments in which a constant high temperature is required, as, for example, in the determination of the vapour density of substances of high boiling-point by V. Meyer's method.

When treated with potassium, diphenylamine yields a solid potassium derivative, $(C_6H_5)_2NK$, the presence of the two phenyl-groups imparting to the $>NH$ group an acidic character.

Triphenylamine, $(C_6H_5)_3N$, may be prepared by heating potassium diphenylamine with bromobenzene at 300° ,

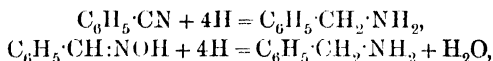


or by heating diphenylamine with iodobenzene in the presence of copper. It is a colourless, crystalline substance, melts at 127° , and does not combine with acids, or with alkyl halides.

Aromatic Amines.

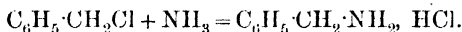
The aromatic amino-compounds, in which the amino-group is united with carbon of the *side-chain*, are of far less importance than those in which the amino-group is united with carbon of the nucleus, and, as will be seen from the following example, they closely resemble the aliphatic amines in chemical properties.

Benzylamine, $C_6H_5 \cdot CH_2 \cdot NH_2$, may be obtained by reducing phenyl cyanide (benzonitrile, p. 453) or benzaldoxime (p. 439),



by treating the amide of phenylacetic acid (p. 462) with bromine and potash,

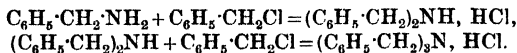
$C_6H_5 \cdot CH_2 \cdot CO \cdot NH_2 + Br_2 + 4KOH = C_6H_5 \cdot CH_2 \cdot NH_2 + 2KBr + K_2CO_3 + 2H_2O$,
and by heating benzyl chloride with alcoholic ammonia,



All these methods are similar to those employed in the preparation of primary aliphatic amines (pp. 211–212).

Benzylamine is a colourless, pungent-smelling liquid, boiling at 184° ; it closely resembles the aliphatic amines in nearly all respects, and differs from the amino-compounds (aniline, toluidine, &c.) in being strongly basic, alkaline to litmus, and readily soluble in water. Like aniline and other primary amines, it gives the carbylamine reaction, but when solutions of its salts are treated with nitrous acid, it is converted into the corresponding alcohol (benzyl alcohol, p. 435), and *not* into a diazonium-salt.

Secondary and tertiary aromatic amines are formed when a primary amine is heated with an aromatic halogen compound, containing the halogen in the *side-chain*; when, for example, benzylamine is heated with benzyl chloride, both *dibenzylamine* and *tribenzylamine* are produced, just as diethylamine and triethylamine are obtained when ethylamine is heated with ethyl bromide,

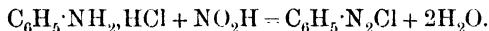


When, therefore, benzyl chloride is heated with alcoholic ammonia, the product contains all three amines and some quaternary base.

CHAPTER XXVII.

DIAZONIUM-SALTS AND RELATED COMPOUNDS.

It has already been stated that when the amino-compounds, in the form of their salts, are treated with nitrous acid in *warm* aqueous solution, they yield phenols; when, however, a *well-cooled*, dilute solution of aniline hydrochloride is treated with nitrous acid, phenol is *not* produced, and the solution contains an unstable substance called *phenyldiazonium chloride* (*diazobenzene chloride*), the formation of which may be expressed by the equation,



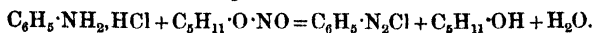
In this respect, then, aniline, and all those amino-compounds which contain the amino-group directly united with carbon of the *nucleus*, differ from other primary amines; the latter are at once converted into alcohols by nitrous acid in the cold, whereas the former are first transformed into diazonium-salts, which, usually only at higher temperatures, decompose more or less readily, with formation of phenols (p. 421).

The *diazo-* or *diazonium-salts* were discovered in 1858 by P. Griess, and may be regarded as salts of *phenyldiazonium hydroxide*, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{OH}$, and its derivatives.

The bases or hydroxides from which these salts are derived are only known in aqueous solution; they cannot be isolated, because they immediately change into highly explosive, very unstable products which seem to be their anhydrides.

The diazonium- (or diazo-) salts may be isolated without much difficulty, and are colourless, crystalline compounds, very readily soluble in water; in the dry state, most of them are *highly explosive*, and should be handled only with the greatest caution.

Diazonium-salts may be obtained *in crystals* by treating a well-cooled solution of an amino-compound in alcohol or acetic acid with amyl nitrite and a mineral acid, so far as possible in the absence of water,



Phenyldiazonium sulphate, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{SO}_4\text{H}$, for example, is prepared as follows: Aniline (5 g.) is dissolved in anhydrous acetic acid (20 g.),

concentrated sulphuric acid (5 g.) is added, the solution is cooled to 20° and pure amyl nitrite (7 g.) is cautiously dropped into the well agitated mixture. As the reaction proceeds, the temperature is lowered to about 10°, and when all the nitrite has been added, the product is kept during 5–10 minutes. On the addition of ether (20–30 c.c.), phenyldiazonium sulphate is precipitated in crystals, which are separated, washed with alcohol and ether, and dried in the air at ordinary temperatures. It is *explosive*.

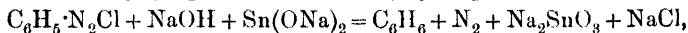
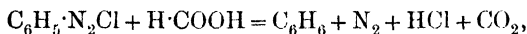
Amyl nitrite is used instead of sodium nitrite as it is soluble in acetic acid or alcohol and is decomposed by sulphuric acid giving nitrous acid.

The diazonium-salts are of very great importance in synthetical chemistry and in the preparation of dyes, because they undergo a number of remarkable reactions; for nearly all purposes for which they are required, however, it is quite unnecessary to isolate the salts, and their aqueous solutions are directly employed.

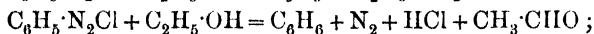
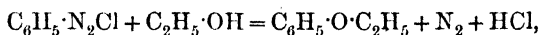
The *preparation of a solution of a diazonium-salt*, therefore, is a very common and a very important operation, and is carried out as follows: The amino-compound is dissolved in an excess ($2\frac{1}{2}$ equivalents) of a dilute mineral acid, the solution is cooled in ice, and an aqueous solution of sodium or potassium nitrite (1 equivalent) is very slowly added to it; this process is known as *diazotisation*, and further details are given later (p. 403).

The more important *reactions* of the diazonium-salts are the following:

When heated with formic acid, or treated with an alkaline solution of sodium stannite, they yield hydrocarbons,



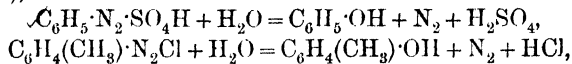
whereas when warmed with alcohol they give an ether and a hydrocarbon, the proportions of which vary with different diazonium compounds,



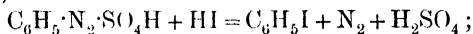
in the decomposition with formic acid or with alcohol, the *anhydrous* salt must be used. Another method for the conversion of a diazonium salt into the corresponding hydrocarbon is given later (p. 406).

When warmed, in aqueous solution, diazonium-salts decompose

rapidly, with the evolution of nitrogen and formation of phenols (p. 421),

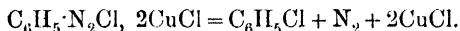


but if warmed with concentrated halogen acids they give halogen compounds,

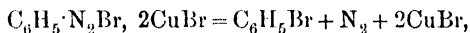


the latter reaction is made use of principally for the preparation of iodo-derivatives (p. 403), because when the other halogen acids are used the product contains a large proportion of the corresponding phenol.

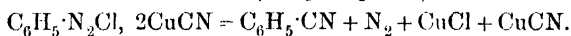
The diazonium-salts behave in a very remarkable way when they are treated with certain cuprous salts; when, for example, a solution of phenyldiazonium chloride is warmed with a solution of cuprous chloride in hydrochloric acid, nitrogen is evolved, but instead of phenol, chlorobenzene is produced. In this reaction the diazonium-salt combines with the cuprous chloride to form a brownish additive compound, which is decomposed at higher temperatures,



If, instead of the chlorides, the corresponding bromides are employed, bromobenzene is produced,



whereas by using a solution of potassium cuprous cyanide, a cyanide or nitrile is formed (compare p. 454),



By means of these very important reactions, which were discovered by Sandmeyer in 1884, it is possible to displace the *diazonium*-group by Cl, Br, (I¹), CN (and indirectly by -COOH, -CHO, and -CH₂·NH₂, into which the -CN group may be converted), and by other atoms or groups. As the diazonium-salts are readily obtainable from amino-compounds, and the latter from nitro-derivatives, Sandmeyer's reaction is very much used in the preparation of halogen, cyanogen, and other derivatives of aromatic compounds in general.

It will be seen from the above statements that the preparation

¹ The use of a cuprous salt is *unnecessary* in the displacement of the diazonium-group by iodine (compare p. 376).

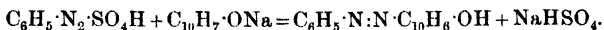
of such derivatives from the amino-compound involves two distinct reactions: firstly, the preparation of a *solution* of the diazonium salt; and, secondly, the decomposition of this salt in a suitable manner.

As an example of the method employed in preparing a solution of the diazonium-salt, the following may serve: Aniline (10 g.) is dissolved in a mixture of concentrated hydrochloric acid (sp. gr. 1.17, 25 g.) and water (about 75 g.), and the solution is cooled by immersing it in coarsely powdered ice; when the temperature has fallen to about 5°, an aqueous solution of sodium nitrite (7.5 g.) is slowly run in from a tap-funnel, the solution being stirred constantly and the temperature kept below 10°. The solution now contains *phenyldiazonium chloride*; if sulphuric had been used instead of hydrochloric acid, *phenyldiazonium sulphate*, $C_6H_5 \cdot N_2 \cdot SO_4H$, would have been formed. The aniline is said to be *diazotised*; diazotisation is complete when the solution contains free nitrous acid (as shown by potassium iodide paper) after it has been stirred well and *left for a short time*. The formation of a *coloured* precipitate at any stage indicates that insufficient acid is present, the precipitate being diazoaminobenzene (p. 408).

If, now, the solution of the diazonium-salt is warmed *alone* nitrogen is evolved and phenol is produced; if treated with potassium iodide, iodobenzene is formed. If it is treated with a cold solution of cuprous chloride in hydrochloric acid, *chlorobenzene* is produced (p. 376), whereas with an aqueous solution of potassium cuprous cyanide, *cyanobenzene* is formed (p. 453). In all these cases the final product is usually separated by distillation in steam.

Gattermann has shown that in many cases the decomposition of the diazonium salts may be brought about by adding copper powder (prepared by the action of zinc-dust on a solution of copper sulphate) to the *cold* acid solution of the salt; when, for example, a solution of phenyldiazonium chloride is treated in this way, nitrogen is evolved and *chlorobenzene* is produced, the reaction being complete in about half an hour.

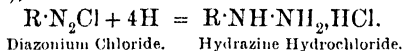
The diazonium-salts react with phenols (p. 420) in alkaline solution and with salts of tertiary aromatic amines (p. 409) giving highly coloured *azo*-compounds, many of which are used in the dyeing industry; when, for example, a solution of a phenyldiazonium-salt is added to an alkaline solution of β -naphthol (p. 485) a scarlet precipitate is formed,



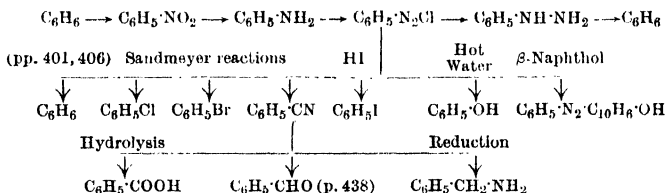
This reaction is often used to prove that a given substance is a primary aromatic amino-compound; the substance is treated with sodium nitrite in acid solution and the product is added to a solution of β -naphthol in an excess of alkali.

The precipitate is not appreciably soluble in alkalis, and for this and other reasons it must be regarded as an isomeride, $C_6H_5 \cdot NH \cdot N : C_{10}H_6 : O$, of the benzene-azo- β -naphthol shown on p. 403.

The diazonium-salts also serve for the preparation of an important class of compounds known as the *hydrazines*; these substances are obtained by reducing the diazonium salts with stannous chloride and hydrochloric acid or some other suitable reagent (p. 405),

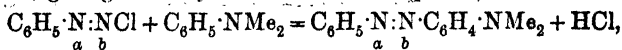


The following scheme summarises some of the principal uses of the diazonium-salts and some general reactions of the aromatic compounds; it should be noted that although benzene is shown here as the parent substance, toluene and other aromatic hydrocarbons (such as naphthalene, p. 475) would undergo similar transformations :

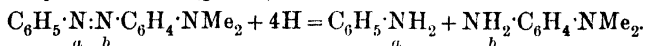


Constitution of Diazonium-Salts.—The state of combination of the two nitrogen atoms and of the acid radical in diazonium-salts has formed the subject of much discussion, and for a long time the view first expressed by Kekulé (1866), that such salts have the constitution, $C_6H_5 \cdot N : NX$ (where $X = Cl, Br, I, NO_3, HSO_4$, &c.), was generally adopted. That only *one* of the two nitrogen atoms is directly united to the nucleus is clearly shown by many facts—as, for example, by the conversion of the diazonium-salts into *mono*-halogen derivatives, *mono*hydric phenols, &c., and by their conversion into hydrazines, such as $C_6H_5 \cdot NH \cdot NH_2$, on reduction (p. 405).

That the acid radical is combined with that nitrogen atom which is *not* directly united to the nucleus *seems* to be proved by many reactions of diazonium-salts—as, for example, the following: Phenyl diazonium chloride reacts readily with dimethylaniline, giving dimethylaminoazobenzene (p. 409),



and this substance, on reduction, yields aniline and dimethyl-*p*-phenylenediamine (p. 397),

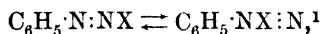


These changes are easily explained on the assumption that the acid radical is attached to the nitrogen atom *b*, but *apparently* they could not take place if the acid radical were united to the nitrogen atom *a*, since, in the latter case, aniline and dimethyl-*p*-phenylenediamine could not be obtained by the reduction of the original product.

There is, however, certain important evidence which does not accord with the above assumption, but which supports the formula, $\text{C}_6\text{H}_5\cdot\text{NX}\text{:N}$, suggested by Blomstrand, in which the acid radical is united to the nitrogen atom *a*: the diazonium salts, like those of strongly basic hydroxides, are not hydrolysed in aqueous solution, but are ionised to an extent comparable with that to which the alkali salts are ionised.

Now, judging from analogy, a hydroxide of the constitution, $\text{C}_6\text{H}_5\cdot\text{N}\text{:N}\cdot\text{OH}$, derived from a salt, $\text{C}_6\text{H}_5\cdot\text{N}\text{:NX}$, would be only feebly basic (as are the oximes, p. 137, for example), whereas a compound, $\text{C}_6\text{H}_5\cdot\text{N}(\text{OH})\text{:N}$, derived from a salt, $\text{C}_6\text{H}_5\cdot\text{NX}\text{:N}$, like a quaternary ammonium hydroxide, $\text{C}_6\text{H}_5\cdot\text{N}(\text{OH})\text{R}_3$, would be a strong base.

Since, therefore, certain reactions of the diazonium salts seem to establish Kekulé's formula, whereas other facts are in favour of Blomstrand's, it is concluded that the salts show tautomerism (p. 189),



and react in one or the other form according to the conditions of the experiment.

The diazonium- (or diazo-) group may therefore be represented by $\text{-N}_2\text{X}$, as in most of the formulæ already used, without indicating further how these atoms are combined with one another.

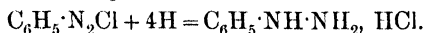
The diazonium-salts are often called diazo-salts, while phenyl-diazonium chloride is termed *diazobenzene* chloride, and so on.

Hydrazines and Hydrazones.

Phenylhydrazine, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{NH}_2$, a compound of great importance, is easily prepared by the reduction of phenyldiazonium

¹ The acid radical in this molecule, like that in ammonium salts, is combined to the nitrogen atom by an *electrovalency* (Part III.).

chloride (E. Fischer), usually with stannous chloride and hydrochloric acid or with sulphur dioxide,

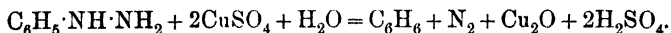


Aniline (9 g.) is dissolved in concentrated hydrochloric acid (170 c.c.), and diazotised in the usual way (p. 403); to the *well-cooled* solution of phenyldiazonium chloride a solution of stannous chloride ($\text{SnCl}_2\cdot 2\text{H}_2\text{O}$, 45 g.) in concentrated hydrochloric acid (100 c.c.) is then slowly added. The precipitate of phenylhydrazine hydrochloride is separated on a suction-filter, washed with a little concentrated hydrochloric acid, and decomposed with an excess of concentrated alkali; the base is extracted with benzene, the extract is dried over solid caustic alkali, and the benzene is distilled. The product may then be purified by distillation under reduced pressure (b.p. about 140° , 60 mm.).

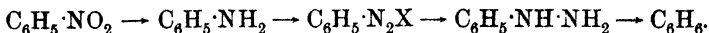
Phenylhydrazine crystallises in colourless prisms, melts at 20° , and boils at 243° , decomposing slightly; it readily undergoes atmospheric oxidation. It is sparingly soluble in cold water, freely so in organic liquids; it is a strong base, and forms well-characterised salts, such as the hydrochloride, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{NH}_2, \text{HCl}$, which is readily soluble in hot water; it reduces Fehling's solution in the cold. Phenylhydrazine is very poisonous; its vapour should not be inhaled and the liquid should not touch the skin.

The *constitution* of phenylhydrazine is established by the fact that, when heated with zinc-dust and hydrochloric acid, the base is decomposed into aniline and ammonia.

Phenylhydrazine is converted into benzene, with the evolution of nitrogen, when it is heated with a solution of copper sulphate or ferric chloride,

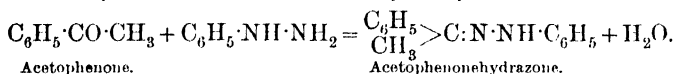
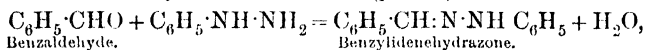


This important reaction may be used in order to change nitrobenzene, aniline, or a diazonium-salt into benzene, since all these compounds may be transformed into phenylhydrazine by the methods already given,



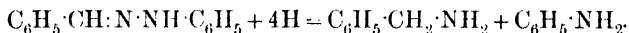
Similar transformations may be brought about in the case of many corresponding aromatic compounds; bromonitrobenzene, for example, may be thus converted into bromobenzene. Further, since the evolution of nitrogen takes place quantitatively when a hydrazine is decomposed with a solution of copper sulphate, this reaction may be employed for the estimation of hydrazines.

Phenylhydrazine reacts readily with aldehydes and ketones, with formation of water and a *phenylhydrazone* (hydrazone); as these compounds are usually sparingly soluble and often crystallise well, they are frequently employed for the identification and isolation of aldehydes and ketones (p. 138),



Many hydrazones are decomposed by strong mineral acids, with regeneration of the aldehyde or ketone, and formation of a salt of phenylhydrazine,

$\text{C}_6\text{H}_5\cdot\text{CH}:\text{N}\cdot\text{NH}\cdot\text{C}_6\text{H}_5 + \text{H}_2\text{O} + \text{HCl} = \text{C}_6\text{H}_5\cdot\text{CHO} + \text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{NH}_2\cdot\text{HCl}$;
on reduction with zinc-dust and acetic acid, they yield primary amines,



The use of phenylhydrazine for the detection and separation of the sugars has already been mentioned (p. 290).

Various derivatives of phenylhydrazine, such as *p*-bromo-, *p*-nitro-, and 2:4-dinitrophenylhydrazine are often used instead of the simple compound, as the hydrazones formed from them crystallise more readily and are more sparingly soluble than the unsubstituted phenylhydrazones.

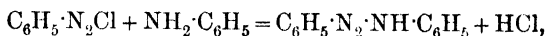
In the preparation of a hydrazone a slight excess of phenylhydrazine is directly added to the aldehyde or ketone, or the two substances are separately dissolved in *dilute* acetic acid, and the solutions are mixed. Very often a reaction takes place spontaneously and in the first case its occurrence is recognised by the development of heat and separation of water; in the case of the dissolved substances, by the separation of an oily, or solid, sparingly soluble precipitate. Sometimes the application of heat is necessary. The hydrazone is separated, washed with dilute acetic acid, and, if a solid, purified by recrystallisation. Phenylhydrazine hydrochloride may be used, instead of the free base, in dilute acetic acid solution, but an excess of sodium acetate must also be added.

The occurrence of a reaction, when a *neutral* substance is treated with phenylhydrazine in the above-described manner, is a very important qualitative test for aldehydes and ketones.

Osazones (p. 290) are prepared by heating a *dilute* aqueous solution of the sugar with an excess of phenylhydrazine acetate; after some time the osazone begins to separate in yellow crystals, and the heating is continued until no further precipitation occurs.

Diazoamino- and Azo-Compounds.

Although some of the more characteristic reactions of the diazonium-salts have already been mentioned, there are numerous other changes of great interest and of great commercial importance which these substances undergo. They react readily with primary, secondary, and tertiary amino-compounds; when, for example, phenyldiazonium chloride is treated with aniline, diazoaminobenzene is formed,



and this compound, with excess of the diazonium-salt, is converted into the di-substitution product, $(\text{C}_6\text{H}_5\cdot\text{N}_2)_2\text{N}\cdot\text{C}_6\text{H}_5$; a secondary base reacts similarly but with one molecule only of the diazonium-salt. With tertiary aromatic amino-compounds, such as dimethylaniline, diazonium-salts react quite differently and give rise to aminoazo-compounds, as shown below.

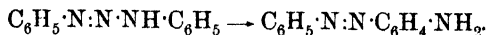
Diazoaminobenzene, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{NH}\cdot\text{C}_6\text{H}_5$, may be described as a typical *diazoamino*-compound; it is formed by the reaction just described.

It is conveniently prepared by treating aniline hydrochloride (5 mols.) with sodium nitrite (about 2 mols.) in very dilute aqueous solution; a part of the aniline is converted into the diazonium-salt, which then reacts with the unchanged aniline, as shown above. The precipitate is separated, washed with water, dried and recrystallised from benzene.

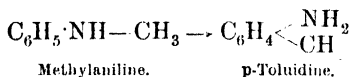
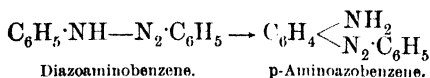
If the precipitate is left in contact with the aqueous solution at 30–40°, it slowly changes into a very dark, pasty or crystalline mass of impure *aminoazobenzene hydrochloride*.

Diazoaminobenzene forms brilliant yellow needles (m.p. 98°), and is sparingly soluble in water, but readily so in alcohol and ether; it is only very feebly basic, and does not form stable salts with acids.

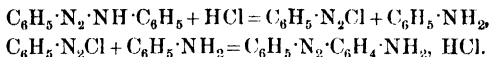
Aminoazobenzene, $\text{C}_6\text{H}_5\cdot\text{N}:\text{N}\cdot\text{C}_6\text{H}_4\cdot\text{NH}_2$, is formed when diazoaminobenzene is warmed with a small quantity of aniline hydrochloride at 40°,



This remarkable reaction, which is a general one, may be compared with that which occurs in the transformation of methylaniline into paratoluidine (p. 396); the group, $-\text{N}_2\cdot\text{C}_6\text{H}_5$, leaves the nitrogen atom and *migrates* to the *para*-position in the nucleus,



In the diazoamino-transformation the presence of hydrochloric or some other strong acid is essential, and the change really takes place in two stages, as follows :



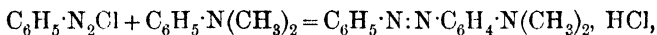
That the group, $-\text{N}_2\cdot\text{C}_6\text{H}_5$, displaces hydrogen from the *p*-position to the $-\text{NH}_2$ group is proved by the fact that the aminoazobenzene thus produced is converted into *para*-phenylenediamine and aniline, on reduction with tin and hydrochloric acid,



Aminoazobenzene may also be prepared by nitrating azobenzene (p. 410), and then reducing with alcoholic ammonium sulphide the *p*-nitroazobenzene, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{C}_6\text{H}_4\cdot\text{NO}_2$, which is thus produced ; these changes are analogous to those which occur in the formation of aniline from benzene—and the formation of aminoazobenzene in this way proves that it is an amino-derivative of azobenzene.

Aminoazobenzene crystallises from alcohol in brilliant orange-red plates, and melts at 127° . Its salts are intensely coloured ; the hydrochloride, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{C}_6\text{H}_4\cdot\text{NH}_2$, HCl, for example, forms beautiful steel-blue needles.

Many other substituted aminoazo-compounds may be obtained *directly* by treating tertiary alkylanilines (p. 397) with diazonium-salts ; dimethylaniline, for example, reacts with phenyldiazonium chloride, yielding dimethylaminoazobenzene hydrochloride,

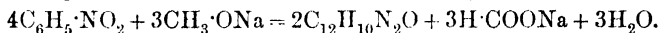


and a diazoamino-compound is not formed as an intermediate product, because dimethylaniline does not contain an $\text{NH}<$ or NH_2- group.

In this case also, the diazo-group, $\text{C}_6\text{H}_5\cdot\text{N}_2-$, takes up the *p*-position to the $\text{N}(\text{CH}_3)_2-$ group, as is shown by the fact that, on reduction, dimethylaminoazobenzene is converted into aniline and dimethyl-*p*-phenylenediamine, the latter being identical with the base which is produced by reducing *p*-nitrosodimethylaniline (p. 397).

Diazonium-salts, as previously stated (p. 403), react very readily with phenols in alkaline solution, giving *hydroxyazo*-compounds, many of which are highly coloured dyes (p. 597). Azo-derivatives formed in this way, and by the interaction of diazonium salts with tertiary amino-compounds, &c., in a similar manner are the products of what is termed a *coupling* process: coupling is a very important operation in the manufacture of azo-dyes.

Azoxybenzene, $C_6H_5 \cdot N : N(O) \cdot C_6H_5$, may be prepared by heating nitrobenzene with a methyl alcoholic solution of sodium methoxide (which gives formaldehyde or sodium formate),



Sodium (1 part) is dissolved in methyl alcohol (25 parts) and nitrobenzene (3 parts) is added; the solution is heated (with reflux condenser) during about 5 hours, the alcohol is distilled, and water added. When sufficiently hard the pasty product is pressed on porous earthenware, left to dry, and crystallised from light petroleum.

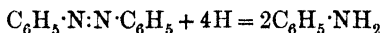
It forms yellow needles, melting at 36° , and is insoluble in water, but readily soluble in most organic liquids.

The constitution of azoxybenzene was at one time represented by the formula, $C_6H_5 \cdot \overset{\text{O}}{\text{N}} \cdot C_6H_5$; it was found, however, that an unsymmetrical azo-compound, $R - N = N - R'$, oxidised with hydrogen peroxide in glacial acetic acid solution, gives structurally isomeric azoxy-compounds, which therefore must be represented by $R \cdot N(O) : NR'$ and $R' \cdot N : N(O)R$ respectively, the oxygen and the nitrogen atoms being united by a *semi-polar* bond (Part III.).

Azobenzene, $C_6H_5 \cdot N : N \cdot C_6H_5$, may be prepared by heating an intimate mixture of azoxybenzene (1 part) and iron filings (3 parts).

The mixture is carefully heated in a small retort, and the solid distillate is purified in the same way as the azoxy-compound.

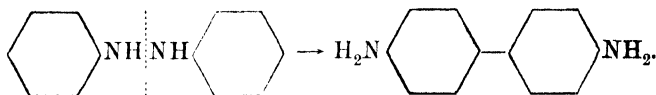
Azobenzene crystallises in brilliant red plates, melts at 68° , and distils at 293° ; it is readily soluble in ether and alcohol, but insoluble in water. Alkaline reducing agents, such as ammonium sulphide, zinc-dust and caustic soda, &c., convert azobenzene into *hydrazobenzene* (p. 411), whereas a mixture of zinc-dust and acetic acid decomposes it, with the formation of aniline,



On oxidation with hydrogen peroxide in glacial acetic acid solution it is converted into azoxybenzene.

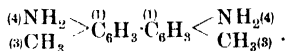
Although azobenzene is of little importance many azo-compounds are manufactured for use as dye stuffs (p. 597).

Hydrazobenzene, $C_6H_5 \cdot NH \cdot NH \cdot C_6H_5$, symmetrical *diphenylhydrazine*, is prepared as above from azobenzene, or directly from nitrobenzene by reduction with zinc-dust and alcoholic sodium hydroxide. It is a colourless, crystalline substance, melting at 131° ; it is readily converted into azobenzene by mild oxidising agents such as mercuric oxide, and slowly even when air is passed through its alcoholic solution. When treated with strong acids, it undergoes a very remarkable isomeric change (the benzidine transformation), and is converted into **pp-diaminodiphenyl**¹ or *benzidine*, a base which is largely used in the preparation of azo-dyes (p. 603),



Benzidine may be produced in one operation by reducing azobenzene with tin and strong hydrochloric acid. It melts at 127° and is very sparingly soluble even in boiling water, but it dissolves readily in diluted (1:1) hydrochloric acid; its *sulphate* forms lustrous scales, very sparingly soluble in boiling water.

Other simple azo-compounds behave just like azobenzene; *o-azotoluene*, $CH_3 \cdot C_6H_4 \cdot N : N \cdot C_6H_4 \cdot CH_3$, for example, may be converted into the corresponding hydrazo-compound, and then, by the benzidine transformation, into *dimethylbenzidine* (tolidine),



N- or β -Phenylhydroxylamine, $C_6H_5 \cdot NH \cdot OH$ (m.p. 82°), is obtained when nitrobenzene is cautiously reduced with zinc dust and water in the presence of ammonium chloride; like hydroxylamine, it is a mono-acidic base. Its hydrochloride, treated with sodium nitrite at 0° in aqueous solution, gives **phenylnitrosohydroxylamine**, $C_6H_5 \cdot N(OH) \cdot NO$ (m.p. 59°), the ammonium salt of which is known as **cupferron**; this salt forms compounds with metals (such as copper and iron), which may differ very considerably in solubility and are therefore very useful in analytical work.

When oxidised with dichromate and dilute sulphuric acid, phenylhydroxylamine yields **nitrosobenzene**, $C_6H_5 \cdot NO$, a crystalline, volatile sub-

¹ The two letters, pp, show that each of the amino-groups is in the para-position to the carbon atom which is directly united to the other phenyl-group.

stance, melting at 68° , which, on oxidation, is converted into nitrobenzene, and on reduction, into aniline.

It has been shown that on reduction, nitrobenzene and, indeed, any aromatic nitro-compound, yields various products according to the reducing agent employed, and the conditions under which the operation is carried out. These changes may be summarised as follows: With *acid*, and *certain* alkaline reducing agents (alcoholic ammonium sulphide), nitrobenzene is reduced first to nitrosobenzene, I, then to phenylhydroxylamine, II, and finally to aniline, III,

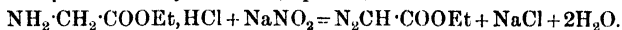
$C_6H_5 \cdot NO_2 \rightarrow (I) C_6H_5 \cdot NO \rightarrow (II) C_6H_5 \cdot NH \cdot OH \rightarrow (III) C_6H_5 \cdot NH_2$; the intermediate compounds, I and II, can only be isolated under very special conditions. With *alkaline* reducing agents, on the other hand, the phenylhydroxylamine and the nitrosobenzene react to form azoxybenzene, IV,

$C_6H_5 \cdot NH \cdot OH + C_6H_5 \cdot NO = (IV) C_6H_5 \cdot N : N(O)C_6H_5 + H_2O$, which may then undergo further reduction successively to azobenzene, V, hydrazobenzene, VI, and finally to aniline,

$(V) C_6H_5 \cdot N : N \cdot C_6H_5 \rightarrow (VI) C_6H_5 \cdot NH \cdot NH \cdot C_6H_5 \rightarrow 2C_6H_5 \cdot NH_2$.

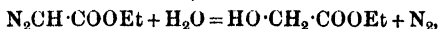
Many of these reactions may also be carried out by electrolytic reduction, the nature of the product depending on the experimental conditions. On the commercial scale azoxybenzene, azobenzene, and hydrazobenzene are all obtained by the graded reduction of nitrobenzene with iron borings and caustic soda.

Diazo-derivatives of Aliphatic Compounds.—Although aliphatic amino-compounds cannot be transformed into diazonium-salts, corresponding with those of the aromatic series, the esters of aliphatic amino-acids may be converted into highly reactive diazo-derivatives (Curtius). When, for example, ethyl aminoacetate, in the form of its hydrochloride, is treated with sodium nitrite in aqueous solution, *ethyl diazoacetate* separates as a yellow oil (b. p. 143°),

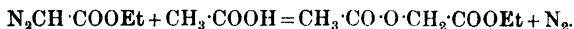
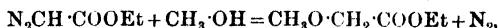


Similar diazo-compounds may be obtained from the esters of other aliphatic amino-acids; most of them have a penetrating odour, and explode when they are heated. In spite of their name, these compounds are not very closely related to the diazonium-salts, but, like the latter, they are readily decomposed, with the elimination of nitrogen.

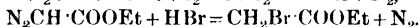
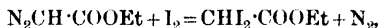
They are transformed into esters of hydroxy-acids when they are boiled with water or dilute acids,



and they give alkyl or acyl derivatives of the hydroxy-esters when they are heated with alcohols and organic acids respectively,



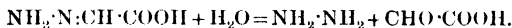
They yield esters of dihalogen substituted acids when they are treated with halogens (even with iodine), and the corresponding monohalogen substitution products with concentrated halogen acids,



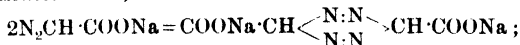
Ethyl diazoacetate gives aminoacetic acid (glycine) and ammonia when it is reduced with zinc-dust and acetic acid, but with ferrous sulphate and caustic soda, or with sodium amalgam and water, it yields a salt of hydraziacetic acid,



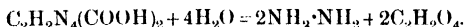
this acid is only stable in the form of its salts, and when the latter are treated with a mineral acid, hydrazine and glyoxylic acid are formed,



Ethyl diazoacetate is hydrolysed by concentrated caustic soda, but the sodium diazoacetate undergoes polymerisation, giving the sodium salt of *bis diazoacetic acid*,

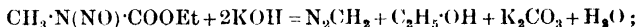


the acid, liberated from this salt, is decomposed by boiling water, giving hydrazine and oxalic acid,



It was in this way that hydrazine was first obtained (Curtius and Jay).

Diazomethane, N_2CH_2 , may be obtained by treating *methylurethane* (p. 203) with nitrous acid in ethereal solution, and then warming the product (*nitrosomethylurethane*) with caustic potash (Pechmann),



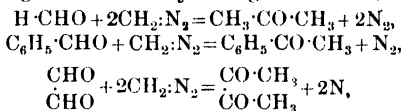
it is more easily prepared from the nitroso-derivative of *methylurea*,



since this substituted urea is produced by the interaction of methylamine hydrochloride and potassium cyanate (p. 321), and is converted into its nitroso-derivative by nitrous acid in aqueous solution.

It is a yellow, odourless, very poisonous gas, and like the aliphatic diazo-esters it is very reactive; although it is hardly attacked by water or by methyl alcohol, it reacts with iodine, hydrochloric acid, and hydrogen cyanide, with the evolution of nitrogen, giving methylene di-iodide, methyl chloride, and methyl cyanide respectively, and reducing agents convert it into *methylhydrazine*, $\text{NH}_2\cdot\text{NH}\cdot\text{CH}_3$. Diazomethane is sometimes used as a *methylating agent*, instead of methyl iodide or dimethyl

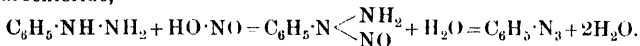
sulphate (p. 179), since it reacts with many compounds containing the group, $-\text{OH}$ or $>\text{NH}$, giving $-\text{OMe}$ or $>\text{NMe}$ respectively, with the evolution of nitrogen; with aldehydes it gives ketones,



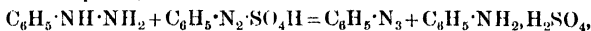
and it converts acids into their methyl esters. The structures of diazo-methane and other aliphatic diazo-compounds are considered in Part III.

Azido-compounds or Azides.—Organic derivatives of azoimide (hydrazoic acid) may be obtained from organic derivatives of hydrazine, just as azoimide itself may be prepared from hydrazine—namely, with the aid of nitrous acid.

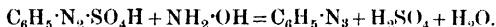
Phenyl azide, $\text{C}_6\text{H}_5\cdot\text{N}_3$ (phenylazoimide), for example, is formed when sodium nitrite is added to an aqueous solution of phenylhydrazine hydrochloride,



It is also produced by the interaction of phenylhydrazine and phenyl-diazonium sulphate,

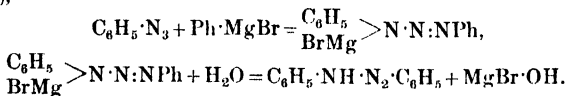


or of phenyldiazonium sulphate and hydroxylamine,



Other azides may be prepared by these general reactions, and also by treating aliphatic halides with sodium or silver azide (see below).

Phenyl azide is a yellow oil, having a very disagreeable and penetrating odour; it may be distilled under greatly reduced pressure, but it explodes when it is heated under the ordinary pressure. It is a very reactive substance; when boiled with dilute sulphuric acid it gives *p*-aminophenol, and with hydrochloric acid, *p*-chloroaniline, nitrogen being evolved in both cases. It combines with the Grignard reagents to give products which are readily converted into diazoamino-compounds (p. 408),



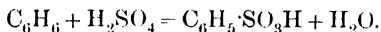
Methyl azide, $\text{CH}_3\cdot\text{N}_3$, the simplest compound of this type, may be obtained by treating sodium azide (sodium azoimide) with dimethyl sulphate; it boils at $20-21^\circ$, and explodes when it is strongly heated. When treated with magnesium methyl iodide it gives diazoaminomethane, $\text{CH}_3\cdot\text{N}\cdot\text{N}\cdot\text{NH}\cdot\text{CH}_3$, a very reactive liquid (b.p. 92°), which is decomposed by acids, giving methylamine, methyl alcohol, and nitrogen.

Ethyl azidoacetate, $\text{N}_3\cdot\text{CH}_2\cdot\text{COOEt}$, prepared from ethyl chloroacetate and sodium azide, **azidoacetic acid**, $\text{N}_3\cdot\text{CH}_2\cdot\text{COOH}$, and many other aliphatic derivatives of azoimide, are known.

CHAPTER XXVIII.

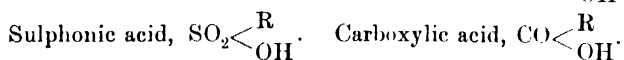
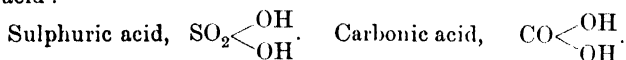
SULPHONIC ACIDS AND THEIR DERIVATIVES.

WHEN benzene is heated with concentrated sulphuric acid it gradually dissolves, and *benzenesulphonic acid* is formed by the substitution of the *sulphonic-group*, $-\text{SO}_3\text{H}$ or $-\text{SO}_2\cdot\text{OH}$, for an atom of hydrogen,

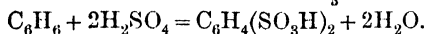
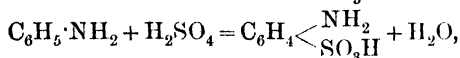
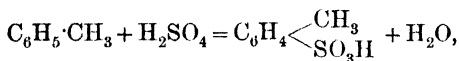


The homologues of benzene, and aromatic compounds in general, behave in a similar manner, and this property of yielding sulphonic derivatives, by the displacement of hydrogen of the *nucleus*, is one of the important characteristics of aromatic, as distinct from aliphatic compounds.

The sulphonic acids are *not* analogous to the alkylsulphuric acids (p. 177), which are hydrogen esters, but they are related to the carboxylic acids, since they may be regarded as derived from sulphuric acid, $\text{SO}_2(\text{OH})_2$, just as the carboxylic acids are derived from carbonic acid, $\text{CO}(\text{OH})_2$ —namely, by the substitution of a hydrocarbon radical for one of the hydroxyl-groups of the acid :



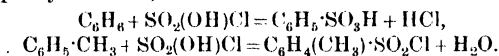
Preparation.—Sulphonic acids are prepared by treating an aromatic compound with sulphuric acid, or with anhydrosulphuric acid,



The number of hydrogen atoms displaced by sulphonic groups depends (as in the case of nitro-groups) on the temperature, on the concentration of the acid, and on the nature of the substance undergoing *sulphonation*

The substance to be *sulphonated* is cautiously added to excess of the acid, and, if necessary, heat is then applied, until the desired change is complete. After being cooled, the product is carefully poured into water, and the acid is isolated, as described later (p. 417). In the case of a substance which is not readily soluble in water or dilute sulphuric acid, it is easy to ascertain when its sulphonation is complete by taking out a small portion of the mixture and adding water; unless the whole is soluble, unchanged substance is still present.

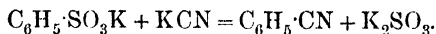
Sometimes chlorosulphonic acid is employed as a sulphonating agent, and in such cases chloroform or carbon tetrachloride may be used as a solvent to moderate the action; the product is either the sulphonic acid or the sulphonyl chloride,



Sulphonic acids are also prepared by the oxidation of *thiophenols* (p. 434) and mercaptans (p. 119).

Properties.—Sulphonic acids, as a rule, are crystalline, readily soluble in water, and often very hygroscopic; they have seldom a definite melting-point, and gradually decompose when heated, so they cannot be distilled. They have a sour taste, a strongly acid reaction, and show, in fact, all the properties of strong acids, their basicity depending on the number of sulphonic-groups in the molecule; their metallic salts (including the barium salts), as a rule, are readily soluble in water.

Although, generally speaking, the sulphonic acids are very stable, and are not decomposed by boiling aqueous alkalis or mineral acids, they undergo certain changes of great importance. When fused with alkalis they yield alkali derivatives of *phenols* (p. 421), and when strongly heated with potassium cyanide, or with potassium ferrocyanide, they are converted into *cyanides* (or nitriles, p. 316), which distil, leaving a residue of potassium sulphite,



The sulphonic-group may also be displaced by hydrogen, by strongly heating the acids alone, or with hydrochloric acid, in sealed tubes, or by passing superheated steam into the acids, or into their solutions in concentrated sulphuric acid.

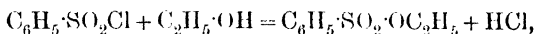
The $-\text{SO}_2\cdot\text{OH}$ group of a sulphonic acid may be transformed into $-\text{SO}_2\text{Cl}$, $-\text{SO}_2\cdot\text{NH}_2$, $-\text{SO}_2\cdot\text{OR}$, &c. by methods similar to those used in preparing the corresponding derivatives of a $-\text{CO}\cdot\text{OH}$ group. When, for example, a sulphonic acid (or its alkali salt)

is treated with phosphorus pentachloride, the hydroxyl-group is displaced by chlorine, and a *sulphonyl chloride* is obtained,

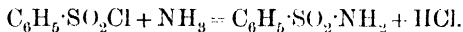


All sulphonic acids behave in this way, and the sulphonyl chlorides are of great value, not only because they are often useful for the isolation and identification of the ill-characterised acids, but also because, like the chlorides of the carboxylic acids (acyl chlorides), they react readily with many other compounds.

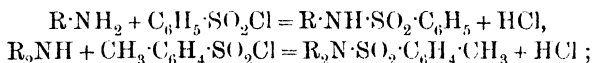
The sulphonyl chlorides are slowly decomposed by water, more rapidly by alkalis, giving the sulphonic acids or their salts; they react with alcohols at high temperatures, yielding esters such as *ethyl benzenesulphonate*,



and when shaken with concentrated ammonia they are converted into *sulphonamides*, which are usually crystalline, have definite melting-points, and often serve for the identification of the acids,



They also react with primary and secondary amines, yielding substituted sulphonamides,



the reaction is often carried out in the presence of alkali (compare p. 453), and the product is usually a well-defined crystalline substance which serves to identify the amine. Mixtures of amines may also be separated with the aid of their sulphonyl derivatives (p. 212).

The isolation of sulphonic acids is very often a matter of some difficulty, because they are readily soluble in water and non-volatile, and cannot be extracted from their aqueous solutions with ether, &c., or separated from inorganic matter by steam distillation. The first step usually consists in their separation from the excess of sulphuric acid employed in their preparation; this may be done in the following manner: The aqueous solution of the product of sulphonation (see above) is boiled with excess of barium (or calcium) carbonate, filtered from the precipitated barium (or calcium) sulphate, and the filtrate—which contains the barium (or calcium) salt of the sulphonic acid—is treated with sulphuric acid so long as a precipitate is produced; an aqueous solution of the sulphonic acid is thus obtained, and when the filtered solution is evaporated to dryness, the acid remains as a syrup or in a crystalline

form. If calcium carbonate has been used, the acid will contain a little calcium salt, which may be got rid of by adding a little alcohol, filtering and again evaporating.

Lead carbonate is sometimes employed instead of barium or calcium carbonate; in such cases the filtrate from the lead sulphate is treated with hydrogen sulphide, filtered from lead sulphide, and then evaporated. These methods, of course, are only applicable provided that the barium, calcium, or lead salt of the acid is soluble in water; in other cases the separation is much more troublesome.

The alkali salts are easily prepared from the barium, calcium, or lead salts by treating the solution of the latter with the alkali carbonate so long as a precipitate is produced, filtering from the insoluble carbonate, and then evaporating.

When two or more sulphonic acids are present in the product, they may often be separated by the fractional crystallisation of their salts; if not, their sulphonyl chlorides are prepared. These compounds are soluble in ether, chloroform, &c., may often be distilled (under reduced pressure), and sometimes crystallise well, so that they may be isolated by the usual methods. (Compare saccharin, p. 455.)

Benzenesulphonic acid, $C_6H_5 \cdot SO_3H$, may be prepared by gently boiling a mixture of equal volumes of benzene and concentrated sulphuric acid on a sand-bath (reflux condenser) during 20–30 hours.

The reaction is at an end when all the benzene has disappeared. The *calcium* (or barium) salt is first isolated, and from the latter the *potassium* salt or the free acid may be prepared (see p. 417).

The acid crystallises with water ($1\frac{1}{2}$ mols.) in colourless plates, and dissolves freely in alcohol; when fused with alkali it yields phenol (p. 425). *Benzenesulphonyl chloride*, $C_6H_5 \cdot SO_2Cl$, melts at 14.5° , the *sulphonamide*, $C_6H_5 \cdot SO_2 \cdot NH_2$, at 150° . Sulphonyl chlorides, as a class, have a characteristic odour, but sulphonamides have no smell.

Benzene-*m*-disulphonic acid, $C_6H_4(SO_3H)_2$, is also prepared by heating the hydrocarbon with concentrated sulphuric acid, but a larger proportion (two volumes) of the acid is employed, and the solution is heated more strongly (or anhydrosulphuric acid is used); when fused with alkalis it yields resorcinol (p. 431).

The three (*o.m.p.*) **toluenesulphonic acids**, $C_6H_4(CH_3) \cdot SO_3H$, are crystalline, and their barium salts are soluble in water; the *o*- and *p*-acids are prepared by sulphonating toluene. ***p*-Toluenesulphonamide**, $C_6H_4(CH_3) \cdot SO_2 \cdot NH_2$ (m.p. 137°), is prepared from the sulphonyl chloride (m.p. 69°), which is a by-product in the manufacture of saccharin (p. 455); with a solution of sodium hypochlorite and sodium hydroxide it gives a salt, $C_6H_4(CH_3) \cdot SO_2 \cdot NNaCl$, known

aschloramine-T, which is a very important antiseptic, used principally for the dressing of wounds.

Sulphanilic acid, $C_6H_4(NH_2) \cdot SO_3H$ (aminobenzene-*p*-sulphonic acid, or aniline-*p*-sulphonic acid), is easily prepared by heating aniline hydrogen sulphate at about 200° for some time.

A slight excess of the theoretical quantity of sulphuric acid is slowly added to aniline, contained in a porcelain basin, and the mixture is constantly stirred as it becomes solid; the basin is then *cautiously* heated on a sand-bath, the contents being stirred, and care being taken to prevent charring. The process is at an end as soon as a small portion of the product, dissolved in water, gives no oily precipitate of aniline on the addition of excess of alkali. When it has cooled, a little water is added to the product, and the sparingly soluble sulphonic acid is separated by filtration, and purified by recrystallisation from boiling water, with the addition of animal charcoal if necessary.

Sulphanilic acid crystallises with water (1 or 2 mols.), and is readily soluble in hot, but only sparingly so in cold, water. It forms salts with bases, but it does not combine with acids; in this respect, therefore, it differs from glycine (p. 202), which forms salts both with acids and bases. Heated strongly with soda-lime it gives aniline, the sulphonic group being displaced by hydrogen, and not by $-ONa$, as is usually the case (p. 416); its diazonium derivative couples with dimethylaniline giving helianthin (p. 601).

Sulphanilamide, $C_6H_4(NH_2) \cdot SO_2 \cdot NH_2$ (*p*-aminobenzenesulphonamide, or *prontosil*), is prepared by sulphonating acetanilide with chlorosulphonic acid, treating the product with ammonia, and then displacing the acetyl group by hydrolysis,



It is very sparingly soluble in water and is of great importance in medicine; more than 200 of its derivatives, many of which, such as *prontosil rubrum*, $NH_2 \cdot SO_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_3(NH_2)_2$, are azo-compounds, have been prepared for the investigation of their therapeutic properties. *Prontosil* kills streptococci and is of immense value in cases of puerperal fever and septicaemia (blood-poisoning); its 2-*pyridyl* derivative, $C_6H_4(NH_2) \cdot SO_2 \cdot NH \cdot C_5H_4N$ (M and B 693), is highly beneficial in pneumonia and spotted fever.

Aminobenzene-m-sulphonic acid (*metanilic acid*) may be obtained by reducing *m*-nitrobenzenesulphonic acid, $C_6H_4(NO_2) \cdot SO_3H$, which is formed by nitrating benzenesulphonic acid or sulphonating nitrobenzene.

Many other sulphonic acids are described later.

CHAPTER XXIX.

PHENOLS.

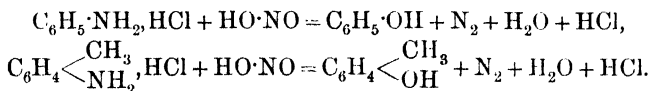
THE hydroxy-compounds of the aromatic series, such as *phenol* or *hydroxy-benzene*, $C_6H_5 \cdot OH$, the *cresols* or *hydroxy-toluenes*, $C_6H_4(CH_3) \cdot OH$, and *benzyl alcohol*, $C_6H_5 \cdot CH_2 \cdot OH$, are derived from the aromatic hydrocarbons by the substitution of hydroxyl-groups for atoms of hydrogen, just as the aliphatic alcohols are derived from the paraffins. It will be seen, however, from the examples just given, that, whereas in the case of benzene, hydrogen atoms of the nucleus must necessarily be displaced, in that of toluene and all the higher homologues this is not so, since the hydroxyl-groups may displace hydrogen either of the *nucleus* or of the *side-chain*. Now the hydroxy-derivatives of benzene, and all those aromatic hydroxy-compounds formed by the substitution of hydroxyl-groups for hydrogen atoms of the *nucleus*, differ in many respects, not only from aliphatic alcohols, but also from those aromatic compounds, which contain the hydroxyl-group in the side-chain; it is convenient, therefore, to make some distinction between the two kinds of aromatic hydroxy-compounds, and for this reason they are classed in two groups, (a) the **phenols**, and (b) the **aromatic alcohols** (p. 435).

The **phenols** are those hydroxy-compounds in which the hydroxyl-groups are united directly with carbon of the *nucleus*; they may be subdivided into monohydric, dihydric, trihydric phenols, &c., according to the number of hydroxyl-groups which they contain. *Phenol*, or *carbolic acid*, $C_6H_5 \cdot OH$, for example, is a monohydric phenol, as are also the three isomeric *cresols* or *hydroxytoluenes*, $C_6H_4(CH_3) \cdot OH$; the three isomeric *dihydroxy-benzenes*, $C_6H_4(OH)_2$, on the other hand, are dihydric phenols, whereas *phloroglucinol*, $C_6H_3(OH)_3$, is an example of a trihydric compound.

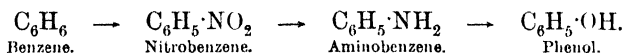
Many of the phenols are easily obtainable, well-known compounds; phenol and the cresols are prepared from coal-tar in large quantities; *carvacrol* and *thymol* occur in various plants; and

catechol, *pyrogallol*, &c. may be obtained by the destructive distillation of certain vegetable products.

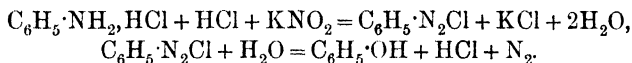
Preparation.—Phenols may be prepared by treating salts of amino-compounds with nitrous acid in aqueous solution, and then heating the solutions until nitrogen ceases to be evolved,



It is possible, therefore, to prepare phenols, not only from the amino-compounds themselves, but also indirectly from the corresponding nitro-derivatives and from the hydrocarbons, since these substances may be converted into amino-compounds,

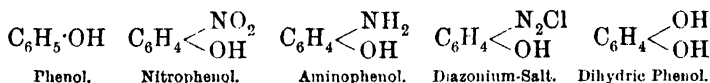


The conversion of an amino-compound into a phenol really takes place in two stages, as already explained (p. 400); at low temperatures the salt of the amino-compound is transformed into a diazonium-salt, but the latter decomposes when its aqueous solution is heated, yielding a phenol,



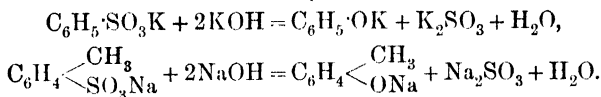
The amino-compound, aniline, for example, is dissolved in dilute hydrochloric acid or sulphuric acid, and *diazotised* in the manner already described (p. 403). The solution of the diazonium-salt is then gradually heated to boiling (reflux condenser) until the evolution of nitrogen (which at first causes a brisk effervescence) is at an end; the phenol is afterwards separated from the tarry matter, which is almost invariably produced, by distillation in steam if possible. In other cases the phenol is extracted with a suitable solvent, and the solution is shaken with caustic alkali, which dissolves out the phenol, leaving most of the impurities in the organic solvent; an excess of an acid is then added and the liberated phenol is isolated by the usual methods.

Dihydric phenols may also be prepared from the monohydric compounds by a corresponding series of changes,



Another important general method for the preparation of phenols consists in *fusing* a salt of a sulphonic acid with a caustic

alkali and then liberating the phenol with a mineral acid; in this case, also, their preparation from the hydrocarbons is often easily accomplished, since the latter are usually converted into sulphonic acids without difficulty,



The alkali salt of the sulphonic acid is placed in an iron—or, better, nickel or silver—basin,¹ together with the solid caustic alkali (about 8 mols.) and a little water, and the basin is heated over a free flame, while the mixture is constantly stirred with a nickel or silver spatula, or with a thermometer, the bulb of which is encased in a glass tube, or covered with a film of silver. As the mixture is very liable to spirt, the eyes of the operator must be protected by spectacles or by a sheet of glass suitably placed. After the alkali and the salt have dissolved, the temperature is slowly raised; as a rule, a temperature considerably above 200° is required, so that if the sulphonic acid is merely boiled with concentrated alkali, the desired change does not occur. When the operation is finished, the fused mass is allowed to cool, dissolved in water, and treated with *excess* of dilute sulphuric acid; the liberated phenol is then isolated in some suitable manner (p. 421).

Dihydric phenols may often be obtained in a similar manner from the disulphonic acids,



Owing to the high temperature at which these reactions must be carried out, secondary changes very frequently occur. When the sulphonic acid contains halogens, the latter are usually displaced by hydroxyl-groups, especially if certain other acid radicals, such as $-\text{NO}_2$, are also present in the molecule; when, for example, *chlorobenzenesulphonic acid*, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{SO}_3\text{H}$, is fused with potash, a dihydric phenol, $\text{C}_6\text{H}_4(\text{OH})_2$, is produced, the halogen as well as the sulphonic-group being displaced. For a similar reason, compounds such as *o*- and *p*-chloronitrobenzene may be converted into the corresponding nitrophenols (p. 426) even by a boiling solution of caustic potash, the presence of the nitro-group facilitating the displacement of the halogen atom; *m*-chloronitrobenzene, on the other hand, is not attacked under these conditions.

In some fusions the process is not one of direct substitution only

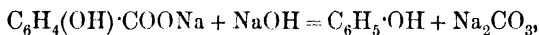
¹ Caustic alkalis readily attack platinum and porcelain at high temperatures, but have little action on nickel and none on silver.

—that is to say, the hydroxyl-groups in the product are not united with the same carbon atoms as those with which the displaced atoms or groups were united; the three (o.m.p.) *bromobenzenesulphonic acids*, for example, all yield some of the *m*-compound, *resorcinol*, $C_6H_4(OH)_2$.

It seems possible that in the case of the *o*- and *p*-di-derivatives one of the substituents is displaced by $-ONa$, and the other by hydrogen, which is formed as the result of a secondary reaction (compare phloroglucinol, p. 433); the sodium phenate thus produced, in the presence of atmospheric oxygen, might then be converted into the sodium derivative of resorcinol.

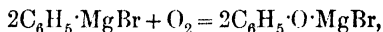


Phenols may also be obtained by heating phenolic acids, such as salicylic acid, with soda-lime.



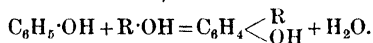
a reaction which is similar to that which occurs in the preparation of the hydrocarbons from the acids.

They may be formed by treating the aryl Grignard reagents (p. 380) with oxygen,



and then decomposing the products with mineral acids.

When phenols are heated with certain aliphatic alcohols at a high temperature (about 200°) in the presence of zinc chloride, the alkyl-group displaces hydrogen of the nucleus,



A phenol may thus be transformed into its higher homologues.

Properties.—Most phenols are colourless, crystalline substances, readily soluble in alcohol and ether; their solubility in water usually increases with the number of hydroxyl-groups in the molecule, while their volatility diminishes; phenol and cresol, for example, are sparingly soluble, distil without decomposing, and are readily volatile in steam, whereas the three dihydric phenols are readily soluble and volatilise very slowly in steam. Alcoholic and aqueous solutions of most monohydric phenols give a violet colouration with ferric salts. The di- and poly-hydric compounds also give colour reactions which vary with the relative positions of the hydroxyl-groups (pp. 431-432).

Most phenols give Liebermann's reaction—that is to say, when dissolved in concentrated sulphuric acid and treated with a nitrosoamine or a nitrite,¹ they yield (red, brown, &c.) solutions which, on the addition of water and excess of alkali, assume an intense blue or green colour. This reaction, therefore, affords a convenient test for phenols as well as for nitrosoamines (p. 396).

Most phenols reduce potassium permanganate solution, and when the alkaline solutions of most di- and poly-hydric phenols are shaken in the air they turn brown or black, owing to the formation of oxidation products.

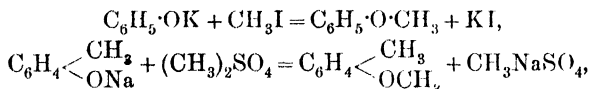
Although the phenols resemble the aliphatic alcohols and also those of the aromatic series in many respects, they differ from the alcohols in several important particulars. The reason for this is that the character of the hydroxyl-group (like that of the amino-group, p. 388) is greatly modified by its union with carbon of the benzene nucleus, just as that of the hydroxyl group in water is altered by combination with acid-forming atoms or radicals, such as Cl- , $\text{NO}_2\text{-}$, &c.; in other words, the phenolic hydroxyl-group has a much more pronounced acidic character than that in alcohols, and for this reason the radicals *phenyl*, $\text{C}_6\text{H}_5\text{-}$, *phenylene*, $\text{C}_6\text{H}_4\text{<}$, &c., may be regarded as acid-forming.

The acidic character of the phenolic hydroxyl-groups is shown by their behaviour towards solutions of the alkali hydroxides, in which phenols dissolve freely, owing to the formation of metallic salts, such as *sodium phenate* or *phenoxide*, $\text{C}_6\text{H}_5\cdot\text{ONa}$, and *potassium cresate*, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{OK}$; these compounds, unlike the metallic derivatives of the alcohols, can exist in presence of water, but are decomposed by carbonic acid and by other acids, with regeneration of the phenols. For these reasons phenols dissolve readily in aqueous alkalis, but are not more soluble in alkali carbonates than in water, unless their molecules contain other acid-forming groups or atoms; *nitrophenol*, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{OH}$, and *picric acid*, $\text{C}_6\text{H}_2(\text{NO}_2)_3\cdot\text{OH}$, for example, are so acidic in character that they decompose the alkali carbonates and dissolve in their aqueous solutions.

The *metallic* derivatives of the phenols, like those of the

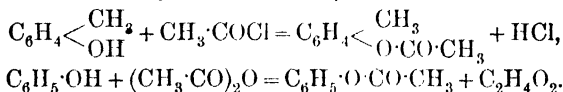
¹ Phenols give with nitrous acid *p*-nitroso-derivatives, which condense with the unchanged phenols to form complex coloured compounds.

alcohols, react with alkyl halides and with dimethyl sulphate (p. 179), yielding substances analogous to the ethers,



which are *not* decomposed by boiling alkalis.

With phosphorus pentachloride and other halides of phosphorus, phenols give, mainly, derivatives of phosphoric or phosphorous acid (p. 374); towards acid chlorides and anhydrides, they behave in much the same way as the alcohols,



When heated with organic or halogen acids, however, the phenols are not changed to any appreciable extent, because, being less basic in character than the alcohols, they do not form esters so readily.

In constitution the phenols may be regarded as somewhat similar to the *tertiary* alcohols, and, like the latter, many of them undergo complex changes on oxidation.

Monohydric Phenols.

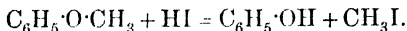
Phenol, $\text{C}_6\text{H}_5\cdot\text{OH}$ (*carbolic acid*, or hydroxybenzene), occurs in very small quantities in human urine and also in that of the ox; it may be obtained from benzene, nitrobenzene, aniline, phenyl-diazonium chloride, benzenesulphonic acid, and salicylic acid (p. 469) by the methods already given; but the phenol of commerce is prepared principally from coal-tar (compare p. 327), in which it was discovered by Runge in 1834.

Phenol crystallises in colourless, deliquescent prisms, which melt at 41° , and turn pink on exposure to air and light; it boils at 183° , and is volatile in steam. It has a very characteristic smell, is highly poisonous, and has a strong caustic action on the skin, quickly causing blisters. It dissolves freely in most organic liquids, but is only moderately soluble (1 part in about 15) in cold water; its neutral *aqueous* solution gives a violet colouration with ferric chloride, and a precipitate of *tribromophenol*, $\text{C}_6\text{H}_2\text{Br}_3\cdot\text{OH}$

(m.p. 92°), with bromine water; both these reactions may serve for the detection of phenol. Owing to its poisonous and anti-septic properties, phenol is extensively used as a disinfectant; it is also employed for the manufacture of picric acid, salicylic acid, phenacetin (p. 427), &c.

When phenol (or cresylic acid, p. 329) is heated with formalin in the presence of ammonia, liquid condensation products are obtained; these mixtures, heated under pressure, change into a *plastic* solid, and finally into a hard infusible and insoluble resin *Bakelite*, which is employed as a substitute for celluloid, shellac, &c., and for the manufacture of a great many useful and ornamental articles (compare pp. 124, 221, 234).

Phenyl methyl ether, $C_6H_5 \cdot O \cdot CH_3$ (*anisole*), may be prepared by heating potassium phenate with methyl iodide or by gradually adding dimethyl sulphate¹ to a solution of sodium phenate in excess of caustic soda; it has a pleasant smell, boils at 152° , and is practically insoluble in water. When warmed with concentrated hydriodic acid, it yields phenol and methyl iodide,



Phenyl ethyl ether, $C_6H_5 \cdot O \cdot C_2H_5$ (*phenetole*), can be obtained from potassium phenate and ethyl iodide; it boils at 172° .

Anisole, phenetole, and other phenolic *ethers* are *not* hydrolysed by boiling alkalis, but like aliphatic ethers, are decomposed by concentrated mineral acids.

Phenyl acetate, $CH_3 \cdot CO \cdot OC_6H_5$, prepared by heating phenol with acetic anhydride, boils at 195° , and is readily hydrolysed even by boiling water.

Nitrophenols, $C_6H_4(NO_2) \cdot OH$, are formed very readily when phenol is treated even with dilute nitric acid; the presence of the hydroxyl-group not only facilitates the introduction of the nitro-group, but also determines the position taken up by the latter (p. 382). The *o*- and *p*-nitrophenols are thus produced.

Phenol (1 part, say 10 g.), just liquefied by the addition of a small proportion of water, is gradually added to a mixture of sodium nitrate (1.6 parts), sulphuric acid (2.5 parts), and water (4 parts), which is kept below 20° and well shaken or stirred. The dark brown, oily product is left to settle, the acid layer is decanted, and the residue is washed with water by decantation; it is then submitted to distillation in steam, whereon *ortho*-nitrophenol passes over as a yellow oil, which crystallises as it cools. The receiver is changed when the distillate ceases to give

¹ As previously stated (p. 179), dimethyl sulphate is very poisonous.

crystals (or oil), but distillation is continued until the whole of the ortho-compound has passed over. The boiling solution of the residue is filtered from tarry matter, and the *para*-nitrophenol, which separates when the solution cools, is purified by recrystallisation from boiling water, with the addition of animal charcoal. The *o*-compound may be crystallised from aqueous alcohol.

m-Nitrophenol is prepared by reducing *m*-dinitrobenzene to *m*-nitroaniline (p. 394), and then treating a solution of the latter in excess of dilute sulphuric acid with nitrous acid; the solution of the diazonium-salt is slowly heated to boiling, and the *m*-nitrophenol, which is thus produced, may be purified by recrystallisation from water.

The melting-points of the three compounds are :

Ortho-nitrophenol,
45°.

Meta-nitrophenol,
96°.

Para-nitrophenol,
114°.

The *o*- and the *m*-compounds are yellow, but the *p*-derivative is colourless; the *o*-compound is readily volatile in steam. The three nitrophenols are all sparingly soluble in cold water, but dissolve freely in alkalis and also in alkali carbonates, forming (*p*-) yellow or (*o*- and *m*-) red salts, which are not decomposed by carbonic acid; they have, therefore, a more marked acidic character than phenol itself, the presence of the nitro-group having an effect comparable with that of the nitro-group in nitric acid.

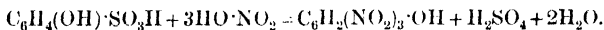
The *ethyl*-derivative of *p*-nitrophenol gives on reduction *p*-aminophenetole, $C_6H_4 \begin{smallmatrix} OC_2H_5 \\ \text{NH}_2 \end{smallmatrix}$ (*phenetidine*), which is converted into its acetyl-derivative when it is treated with acetic anhydride. The product, *acetyl-p*-phenetidine, $C_6H_4 \begin{smallmatrix} OC_2H_5 \\ NHAc \end{smallmatrix}$ (*acetyl-p*-aminophenetole), melts at 135°, is only very sparingly soluble in water, and is used in medicine, under the name, *phenacetin*, in cases of neuralgia, and as an antipyretic.

Picric acid, $C_6H_2(NO_2)_3 \cdot OH$ (trinitrophenol), is formed when materials such as wool, silk, leather, and some resins are heated with concentrated nitric acid, very complex reactions taking place; it may be obtained by heating phenol, or the *o*- and *p*-nitrophenols, with nitric and sulphuric acids.

Phenol (1 part) is dissolved in concentrated sulphuric acid (5 parts), water (4 parts) is added, the solution is cooled, and nitric acid of sp. gr. 1.4 (4 parts) is cautiously dropped in, the mixture being well shaken; after the first energetic action has subsided, the solution is carefully heated on a water-bath during about two hours, and then

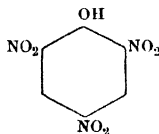
allowed to cool. The product solidifies to a mass of crystals; it is mixed with a little water, separated by filtration, washed, and recrystallised from hot water.

When phenol is dissolved in sulphuric acid, it is converted into a mixture of *o*- and *p*-phenolsulphonic acids, $C_6H_4(OH) \cdot SO_3H$ (p. 429); on subsequent treatment with nitric acid, the sulphonie-group, as well as two atoms of hydrogen, are displaced by nitro-groups,



Picric acid is a yellow crystalline compound, melting at 122.5° . It is only very sparingly soluble in cold, but is moderately easily soluble in hot water, and its solutions impart to silk and wool, but not to cotton, a yellow colour; it is, in fact, one of the earlier known artificial organic dyes. It has very marked acidic properties, and readily decomposes carbonates. The *potassium* derivative, $C_6H_2(NO_2)_3 \cdot OK$, and the *sodium* derivative, $C_6H_2(NO_2)_3 \cdot ONa$, are yellow crystalline compounds, the former being sparingly, the latter readily, soluble in cold water. These compounds, and also the ammonium derivative, *explode* violently on percussion or when heated; picric acid itself burns quietly when it is ignited on a spatula, but can be caused to explode violently with a detonator, and has been used in warfare under the name of *Melinite* or *Lyddite*. When warmed with an aqueous suspension of bleaching powder, picric acid is completely decomposed, giving chloropicrin (p. 73).

Picric acid may be produced by oxidising 1:3:5-*trinitrobenzene*, $C_6H_3(NO_2)_3$, with potassium ferricyanide, the presence of the nitro-groups facilitating the substitution of hydroxyl for hydrogen; the constitution of picric acid, therefore, is represented by the formula,

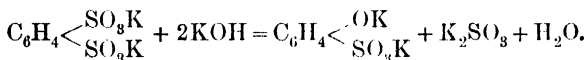


which is usually written $C_6H_2(NO_2)_3 \cdot OH$, $[3NO_2 = 2:4:6]$ (compare footnote, p. 385).

Picric acid forms crystalline compounds with benzene, naphthalene, anthracene, and other hydrocarbons, and also with amines (p. 199), so that it may be used for the detection, or purification, of such substances. The compound which it forms with benzene, for example, crystallises in yellow needles, is decomposed by water, and has the composition, $C_6H_2(NO_2)_3 \cdot OH, C_6H_6$; *ethylamine picrate*, $C_2H_5 \cdot NH_2, C_6H_2(NO_2)_3 \cdot OH$, and the picrates of other bases may be recrystallised from water.

Phenol-o-sulphonic acid, $C_6H_4(OH) \cdot SO_3H$, is formed, together with a comparatively small quantity of the *p*-acid, when a solution of phenol in concentrated sulphuric acid is kept for some time at ordinary temperatures; when, however, the solution is heated at $100-110^\circ$, the *o*-acid is decomposed into phenol and sulphuric acid, which then react to give *phenol-p-sulphonic acid*.

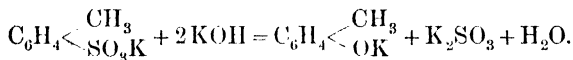
Phenol-m-sulphonic acid is prepared by carefully heating benzene-*m*-disulphonic acid with alkali at $170-180^\circ$; under these conditions only one of the sulphonic-groups is displaced,



The *o*-acid is used as an antiseptic under the name, *aseptol*.

The three (*o.m.p.*) **cresols**, $C_6H_4(CH_3) \cdot OH$ (hydroxytoluenes), the next homologues of phenol, occur in coal-tar, from which the *o*-compound can be isolated by fractional distillation; for the separation of the *m*- and *p*-isomerides from one another, chemical methods must be used.

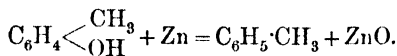
They may be prepared by diazotising the corresponding *toluidines* (aminotoluenes), $C_6H_4(CH_3) \cdot NH_2$, or by fusing the corresponding *toluenesulphonic acids* with potash,



Their melting- and boiling-points are given below.

	Ortho-cresol.	Meta-cresol.	Para-cresol.
M.p.	31°	11°	36°
B.p.	191°	202°	201°

The **cresols** resemble phenol in most ordinary properties, as, for example, in being only moderately soluble in water, and in forming potassium and sodium derivatives, which are decomposed by carbonic acid; they also yield alkyl-derivatives, &c., by the displacement of the hydrogen of the hydroxyl-group. They all give a bluish colouration with ferric chloride, and on distillation with zinc-dust, they are all converted into toluene,

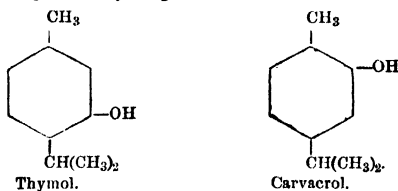


Like phenol, the **cresols** are poisonous and are used as antiseptics (*Lysol*), as is also *amyl-m-cresol*.

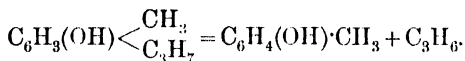
A very interesting fact regarding the three **cresols** is that they are not oxidised by chromic acid, although toluene, as already

stated, is slowly converted into benzoic acid; the presence of the hydroxyl-group, therefore, protects the methyl-group from the attack of acid oxidising agents, and this is true also in the case of other phenols of similar constitution. If, however, the hydrogen of the hydroxyl-group is displaced by an alkyl, or by an acyl-radical, then the protection is withdrawn, and the methyl- is converted into the carboxyl-group in the usual manner; the *methylcresols*, $C_6H_4(OCH_3) \cdot CH_3$, for example, are oxidised by chromic acid, and are converted into the corresponding *methoxybenzoic acids*, $C_6H_4(OCH_3) \cdot COOH$.

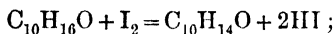
Of the higher monohydric phenols, **thymol** and **carvacrol** may be mentioned; these two compounds are isomeric monohydroxy-derivatives of *cymene*, $C_6H_4(CH_3) \cdot C_3H_7$ (p. 369), and their constitutions are respectively represented below:



Thymol occurs in oil of thyme, together with *cymene*; it crystallises in large plates, melts at 51.5° , and has a characteristic smell, like that of thyme. It is only very sparingly soluble in water, and does *not* give a colouration with ferric chloride; when heated with phosphoric anhydride, it yields propylene and *m*-cresol,



Carvacrol occurs in the oil of *Origanum hirtum*, and may be prepared by heating camphor with iodine,

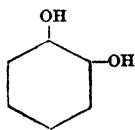


it is an oil boiling at 236° , and its alcoholic solution gives a green colouration with ferric chloride. When heated with phosphoric anhydride, it is decomposed into propylene and *o*-cresol.

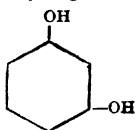
Dihydric Phenols.

The isomeric dihydric phenols—*catechol*, *resorcinol*, and *quinol* (hydroquinone)—are well-known compounds of considerable

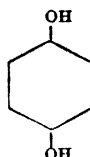
importance, and are respectively represented by the formulæ,



Catechol
(Ortho-dihydroxybenzene).

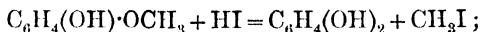


Resorcinol
(Meta-dihydroxybenzene).



Quinol (Hydroquinone)
(Para-dihydroxybenzene).

Catechol, $C_6H_4(OH)_2$, occurs in *catechu*, a substance obtained in India from *Acacia catechu* and other trees, and was first obtained by the dry distillation of this vegetable product. It may be obtained by fusing *phenol-o-sulphonic acid* with potash, and by heating *guaiacol* or *methylcatechol* (see below) with concentrated hydriodic acid,



also by oxidising salicylaldehyde with a dilute alkaline aqueous solution of hydrogen peroxide. It is prepared commercially by heating *o*-chlorophenol with 20 per cent. alkali and a trace of copper sulphate at about 190° under pressure. It is colourless, melts at 104° , and is readily soluble in water. Its solutions in aqueous alkalis darken on exposure to the air; its aqueous solution gives, with ferric chloride, a *green* colouration, which, on the addition of sodium bicarbonate, changes first to violet and then to red, a reaction which is common to many *ortho*-dihydric phenols (p. 434).

Guaiacol, $C_6H_4(OMe) \cdot OH$, is obtained from the tar produced during the destructive distillation of beech-wood; it melts at 28° , has a pleasant smell, and gives a green colouration with ferric chloride in alcoholic solution. ✓

Resorcinol, $C_6H_4(OH)_2$, is prepared on a large scale by fusing benzene-*m*-disulphonic acid with sodium hydroxide,

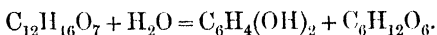


It is also obtained when the *p*-disulphonic acid and many other *o*- and *p*-di-derivatives of benzene are treated in the same way, but how such remarkable changes occur, it is difficult to say (compare p. 423). Resorcinol melts at 111° , and dissolves freely in water, alcohol, and ether; its aqueous solution gives a dark-violet colouration with ferric chloride, and a crystalline precipitate of *tribromoresorcinol*, $C_6HBr_3(OH)_2$, with bromine water. When resorcinol is strongly heated for a few minutes with phthalic

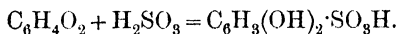
anhydride (p. 458), and the brown or red mass is then dissolved in caustic soda, there results a brownish-red solution, which, when poured into a large volume of water, shows a beautiful green fluorescence; this phenomenon is due to the formation of *fluorescein*. Other *m*-dihydric phenols give this *fluorescein reaction*, which, therefore, affords a convenient and very delicate test for such compounds; the fluorescein reaction may also be employed as a test for *inner* anhydrides of *dicarboxylic acids* (p. 247).

Resorcinol is used in large quantities in preparing *fluorescein*, *eosin*, and various azo-dyes (p. 592).

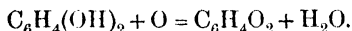
✓ **Quinol**, $C_6H_4(OH)_2$ (hydroquinone), is formed, together with glucose, when the glucoside (footnote, p. 310), *arbutin*, which occurs in the leaves of the bear-berry, is boiled with dilute sulphuric acid,



It is usually prepared by reducing quinone (p. 445) with sulphurous acid in aqueous solution,¹ but about 20 per cent. of the quinone is converted into *quinolsulphonic acid*,



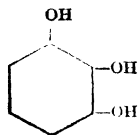
It melts at 169°, is readily soluble in water, and when treated with ferric chloride or other mild oxidising agents, it is converted into quinone,



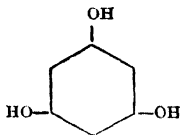
Its solutions in aqueous alkalis darken on exposure to the air.

Trihydric Phenols.

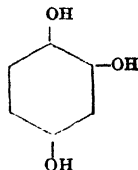
The three trihydric phenols, $C_6H_3(OH)_3$, are respectively represented by the following formulæ:



Pyrogallol.
1:2:3-Trihydroxybenzene.



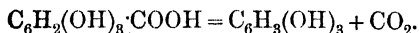
Phloroglucinol.
1:3:5-Trihydroxybenzene.



Hydroxyquinol.
1:2:4-Trihydroxybenzene.

¹ The name *hydroquinone*, by which this dihydroxybenzene is still known, recalls its relation to quinone; it was changed to *quinol*, in conformity with the rule that the name of a hydroxy-compound should end in *ol*.

Pyrogallol, $C_6H_3(OH)_3$, sometimes called pyrogallic acid, is prepared by heating gallic acid (p. 472) alone or with glycerol, at about 210° , until the evolution of carbon dioxide ceases,



It is colourless, melts at 132° , and is readily soluble in water, but more sparingly soluble in alcohol and ether (the effect of hydroxyl-groups); its aqueous solution gives, with ferric chloride, a red, and with ferrous sulphate containing a trace of ferric chloride, a deep, dark-blue colouration. It dissolves freely in alkalis, giving solutions which rapidly absorb oxygen and turn black (even on exposure to the air), a fact which is made use of in gas analysis, for the estimation of oxygen. Pyrogallol has powerful reducing properties, and precipitates gold, silver, and mercury from solutions of their salts, being itself oxidised to oxalic acid and other products; many other phenols, such as *catechol*, *resorcinol*, and *quinol*, are also reducing agents, especially in alkaline solution, but the monohydric-compounds are much less readily oxidised. Pyrogallol and quinol are used in photography as developers. Aminomonohydric phenols and their derivatives are also employed. *Metol* contains the sulphate of *p*-methylaminophenol, $C_6H_4(OH) \cdot NH \cdot CH_3$, and *amidol* the sulphate of *diaminophenol* [$OH:2NH_2:1:2:4$].

Pyrogallol forms mono-, di-, and tri-alkyl-derivatives; the *dimethyl*-derivative, $C_6H_3(OCH_3)_2 \cdot OH$, occurs in beech-wood tar.

Phloroglucinol, $C_6H_3(OH)_3$ (1:3:5- or symmetrical tri-hydroxy-benzene), is produced when phenol, resorcinol, and many resins, such as gamboge, dragon's-blood, &c., are fused with alkali, and is prepared by the hydrolysis of 1:3:5-triamino-benzene (p. 385).

It may also be prepared by fusing resorcinol (1 part) with caustic soda (6 parts) during about twenty-five minutes, or until the vigorous evolution of hydrogen has ceased. The chocolate-coloured melt is dissolved in water, and the solution is treated with excess of dilute sulphuric acid and repeatedly extracted with ether; the extract is evaporated, and the residue recrystallised from water.

It crystallises with $2H_2O$ in colourless prisms, melts at about 218° , and is very soluble in water; the solution has a sweet taste, gives with ferric chloride a bluish-violet colouration, and when mixed with caustic alkali, it rapidly turns brown in contact with the air, owing to the absorption of oxygen. When warmed with acetyl

chloride, phloroglucinol yields a *triacetate*, $C_6H_3(C_2H_3O_2)_3$, melting at 106° , and in many other reactions its behaviour points to the conclusion that it contains three *hydroxyl*-groups; on the other hand, when treated with hydroxylamine, it gives a *trioxime*, $C_6H_6(:N\cdot OH)_3$, and in this and certain other respects it behaves as though it were a *triketone*.

For these reasons phloroglucinol may be represented by one of the following formulæ:

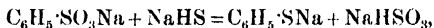


and it may be assumed that the *trihydroxy*-compound is readily convertible into the *triketone* and *vice versa* by tautomeric change (compare p. 189).

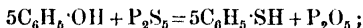
Hydroxyquinol, or 1:2:4-trihydroxybenzene, is formed when quinol is fused with potash. It melts at 140° , is very soluble in water, and its aqueous solution is coloured greenish-brown by ferric chloride, but on the addition of sodium bicarbonate the colour changes to blue and then to red (p. 431).

Thiophenols and Sulphides.

Thiophenol, *phenyl mercaptan*, $C_6H_5\cdot SH$, may be obtained by heating sodium benzenesulphonate with sodium hydrogen sulphide,



or by treating phenol with phosphorus pentasulphide,



it is usually prepared by reducing benzenesulphonyl chloride with zinc and dilute sulphuric acid,



It boils at 169° and has a most unpleasant smell; it resembles ethyl mercaptan in forming a mercury derivative, $(C_6H_5\cdot S)_2Hg$, and in being oxidised to a sulphonic acid (p. 119).

Diphenyl sulphide, $(C_6H_5)_2S$, is formed, together with thiophenol, by treating phenol with phosphorus pentasulphide (above). It boils at 292° and has a smell of leeks. It can be oxidised to *diphenyl sulphone*, $(C_6H_5)_2SO_2$ (compare p. 119). Other mercaptans and sulphides can be obtained by similar reactions and have similar properties.

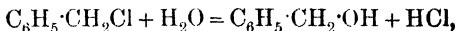
CHAPTER XXX.

ALCOHOLS, ALDEHYDES, KETONES, AND QUINONES.

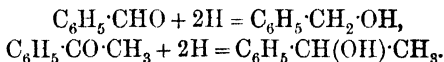
Alcohols.

THE aromatic alcohols are derived from the hydrocarbons by the substitution of hydroxyl-groups for hydrogen atoms of the *side-chain*: *benzyl alcohol*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{OH}$, for example, is derived from *toluene*; *tolyl carbinol*, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{CH}_2\cdot\text{OH}$, from *xylene*; and so on. The compounds of this type are very closely related to the alcohols of the aliphatic series, although, of course, they show at the same time the general behaviour of aromatic substances.

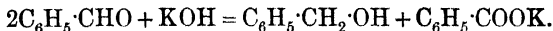
They may be obtained by methods exactly analogous to those employed in the case of the aliphatic alcohols—namely, by heating the corresponding halogen derivatives with water, weak alkalis, or moist silver oxide (p. 69),



and by reducing the corresponding aldehydes and ketones,



Those compounds which, like benzyl alcohol, contain the carbinol-group, $-\text{CH}_2\cdot\text{OH}$, directly united with the benzene nucleus, may also be prepared by treating the corresponding aldehydes with alcoholic or aqueous caustic potash,



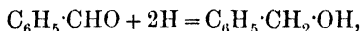
In this reaction *benzyl benzoate*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{O}\cdot\text{CO}\cdot\text{C}_6\text{H}_5$, is probably formed in the first place.

The aromatic alcohols are usually colourless liquids, very sparingly soluble in water; their behaviour with alkali metals, phosphorus pentachloride, and acids, is similar to that of the aliphatic compounds, as will be seen from a consideration of the properties of benzyl alcohol, one of the better-known aromatic alcohols.

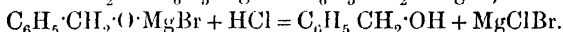
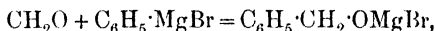
Benzyl alcohol, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{OH}$ (phenylcarbinol), an isomeride of the three *cresols* (p. 429), occurs in storax (a resin obtained from the tree, *Styrax officinalis*), and also in balsam of Peru and balsam

of Tolu, either in the free state, or as an ester in combination with cinnamic or benzoic acid.

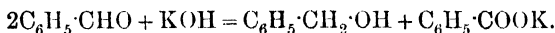
It may be obtained by reducing benzaldehyde (p. 437) with sodium amalgam and water,



and by passing dry formaldehyde into an ethereal solution of magnesium phenyl bromide and then decomposing the additive compound with acids,

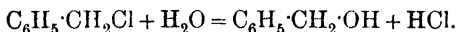


It is conveniently prepared in the laboratory by treating benzaldehyde with cold caustic potash (Cannizzaro's reaction),



The aldehyde (10 parts) is shaken with the solution of potash (9 parts) in water (10 parts) until the whole forms an emulsion, which is allowed to stand during twenty-four hours; water is then added to dissolve the potassium benzoate, the solution is extracted with ether, the dried ethereal extract is evaporated, and the benzyl alcohol is purified by distillation.

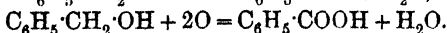
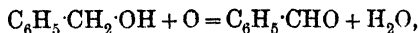
It is produced commercially by boiling benzyl chloride with milk of lime or a solution of sodium carbonate,



Benzyl alcohol is a colourless liquid, boiling at 206° ; it is only sparingly soluble in water, but is miscible with organic solvents in all proportions. It is readily acted on by sodium and potassium, with evolution of hydrogen, yielding metallic derivatives, which are decomposed by water, and when treated with phosphorus pentachloride, it is partly converted into *benzyl chloride*,



When heated with concentrated acids, or treated with anhydrides or acid chlorides, it gives esters; with hydrobromic acid, for example, it yields *benzyl bromide*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\text{Br}$ (b.p. 199°), and with acetyl chloride or acetic anhydride it gives *benzyl acetate*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{O}\cdot\text{CO}\cdot\text{CH}_3$ (b.p. 216°). On oxidation with dilute nitric acid, it is first converted into benzaldehyde and then into benzoic acid,



All these changes are strictly analogous to those undergone by the aliphatic alcohols.

A great many alcohols containing both aliphatic (alkyl) and aromatic (aryl) hydrocarbon radicals have been prepared with the aid of the Grignard reagents. *Phenyldimethyl carbinol*, $C_6H_5 \cdot C(CH_3)_2 \cdot OH$, for example, is easily obtained from acetone and magnesium phenyl bromide (p. 380); *phenylethyl carbinol*, $C_6H_5 \cdot CH(C_2H_5) \cdot OH$, from benzaldehyde and magnesium ethyl bromide, and so on. In all such compounds the hydroxyl-group shows much the same behaviour as that in aliphatic tertiary and secondary alcohols respectively.

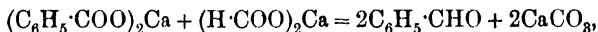
Aldehydes.

The relation between the aromatic aldehydes and the aromatic alcohols is the same as that which exists between the corresponding classes of aliphatic compounds, that is to say, the aldehydes are formed from the primary alcohols by the oxidation of the $-CH_2 \cdot OH$ group; *benzaldehyde*, $C_6H_5 \cdot CHO$, for example, corresponds with *benzyl alcohol*, $C_6H_5 \cdot CH_2 \cdot OH$; *salicylaldehyde*, $C_6H_4(OH) \cdot CHO$, with *salicyl alcohol*, $C_6H_4(OH) \cdot CH_2 \cdot OH$; *phenyl-acetaldehyde*, $C_6H_5 \cdot CH_2 \cdot CHO$, with β -*phenylethyl alcohol* (*benzyl carbinol*), $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot OH$, and so on.

Now those compounds, which contain an aldehyde-group directly united with carbon of the *nucleus*, are of far greater importance than those in which the aldehyde-group is combined with a carbon atom of the *side-chain*; whereas, moreover, the latter resemble aliphatic aldehydes very closely in general character, and do not therefore require a detailed description, the former differ from the aliphatic compounds in several important particulars. This will be seen from the following account of *benzaldehyde* and *salicylaldehyde*, two of the better-known aromatic compounds, which contain the aldehyde-group directly united with the benzene *nucleus*.

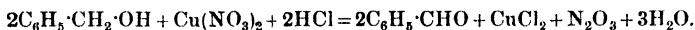
Benzaldehyde, $C_6H_5 \cdot CHO$, sometimes called 'oil of bitter almonds,' was formerly obtained from the glucoside, *amygdalin* (compare p. 310), which occurs in the almonds together with, but apart from, an enzyme, emulsin; when the almonds are macerated with water, the emulsin gradually decomposes the amygdalin into benzaldehyde, hydrogen cyanide, and glucose.

Benzaldehyde may be obtained by oxidising benzyl alcohol with dilute nitric acid, and by heating a mixture of calcium benzoate and calcium formate,



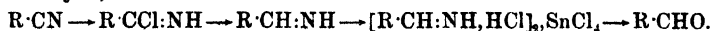
reactions analogous to those employed in the aliphatic series.

It may be prepared in the laboratory by boiling benzyl chloride with an aqueous solution of lead nitrate, or copper nitrate, the benzyl alcohol which is first formed being oxidised to the aldehyde by the metallic nitrate,



Benzyl chloride (5 parts), water (25 parts), and copper nitrate (4 parts) are placed in a flask connected with a reflux condenser, and the mixture is boiled during six to eight hours, a stream of carbon dioxide being passed into the liquid all the time, in order to expel the oxides of nitrogen, which would otherwise oxidise the benzaldehyde to benzoic acid. The process is at an end when the oil contains only traces of chlorine, which is ascertained by washing a small portion with water, and boiling it with silver nitrate and nitric acid. The benzaldehyde is then extracted with ether, the ethereal extract is shaken with a concentrated solution of sodium bisulphite, and the crystals of the bisulphite compound, $\text{C}_6\text{H}_5\cdot\text{CHO}$, NaHSO_3 , are separated by filtration and washed with ether; the benzaldehyde is then regenerated, with the aid of dilute sulphuric acid, extracted with ether, dried, and distilled.

A general method for the preparation of aromatic (and also aliphatic) aldehydes, is the reduction of a cyanide to an aldimine with a solution of anhydrous stannous chloride in ether, saturated with hydrogen chloride; the stannichloride of the aldimine, which is precipitated, is readily decomposed by warm water, giving the aldehyde,



Since cyanides can be obtained from diazonium salts (p. 402), this method is of considerable importance in the laboratory.

Benzaldehyde is usually prepared on the large scale by (a) the direct oxidation of toluene or by (b) the hydrolysis of benzal chloride, $\text{C}_6\text{H}_5\cdot\text{CHCl}_2$ (p. 379).

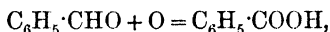
(a) Toluene is cautiously oxidised at about 40° with 65 per cent. sulphuric acid and precipitated manganese dioxide. (b) Crude benzal chloride (benzylidene dichloride, p. 379), which contains benzotrichloride, is heated at 30° and stirred with about 0.3 per cent. of iron powder; after about 30 minutes, 15 per cent. of water is added and the temperature is carefully raised, whereon the dichloride undergoes hydrolysis.

The benzoic acid, formed from the trichloride, is neutralised with milk of lime, the benzaldehyde is distilled in steam, agitated with a 35 per cent. solution of sodium bisulphite until it has all dissolved, and then liberated from the clarified solution by the addition of sodium carbonate.

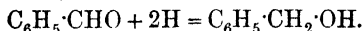
In another process it is prepared directly from benzene by passing a mixture of carbon monoxide and hydrogen chloride into the hydrocarbon, in the presence of anhydrous cuprous chloride and aluminium chloride (Gattermann). This method seems to depend on the formation of the very unstable chloride of formic acid, $\text{H}\cdot\text{CO}\cdot\text{Cl}$, which, in the presence of the aluminium chloride, reacts with the benzene, with elimination of hydrogen chloride; many other aromatic aldehydes may be prepared from other hydrocarbons by this method.

Benzaldehyde is a colourless, highly refractive liquid of sp. gr. 1.05 at 15° ; it boils at 179° , and is volatile in steam. It has a pleasant smell, like that of bitter almonds, and is only sparingly soluble in water, but is miscible with organic liquids in all proportions. It is extensively used for flavouring purposes, and is employed, on the large scale, in the manufacture of various dyes.

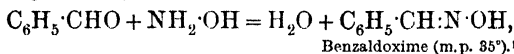
Benzaldehyde, and aromatic aldehydes in general, *resemble* the aliphatic aldehydes in the following respects: They readily undergo oxidation, sometimes merely on exposure to the air, yielding the corresponding acids,



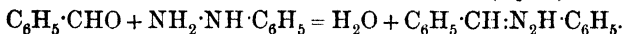
and they reduce ammoniacal solutions of silver hydroxide, but in some cases only very slowly. On reduction they are converted into the corresponding alcohols,



When treated with phosphorus pentachloride, they give dihalogen derivatives, such as benzal chloride, $\text{C}_6\text{H}_5\cdot\text{CHCl}_2$, two atoms of chlorine being substituted for one atom of oxygen. They react with hydroxylamine, yielding aldoximes, and with phenylhydrazine, giving hydrazones,



Benzaldoxime (m.p. 35°).¹



Benzylidenehydrazone (m.p. 159°).²

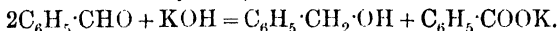
¹ There are two isomeric benzaldoximes (Part III.).

² This compound is also called benzalphenylhydrazone.

They also react with semicarbazide (p. 241). *Benzaldehyde semicarbazone*, $\text{NH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{N}\cdot\text{CH}\cdot\text{C}_6\text{H}_5$ (m.p. 214°), for example, separates at once in crystals when benzaldehyde is shaken with an aqueous solution of semicarbazide hydrochloride and sodium acetate. Like some hydrazones, the semicarbazones are decomposed by acids, yielding the aldehyde or ketone and a salt of semicarbazide.

They show Schiff's reaction (p. 128), combine directly with sodium bisulphite, forming crystalline compounds, and with hydrogen cyanide they yield hydroxycyanides, or cyanohydrins, such as *mandelonitrile*, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{CN}$.

Benzaldehyde, and other aromatic aldehydes which contain the $-\text{CHO}$ group directly united with the benzene nucleus, differ from the fatty aldehydes in the following respects: They do not reduce Fehling's solution, and they do not readily undergo polymerisation; when shaken with concentrated potash (or soda), they yield a mixture of the corresponding alcohol and acid (Cannizzaro's reaction, p. 436),

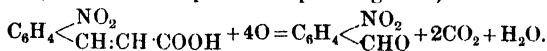


They do not readily form additive compounds with ammonia, but yield complex products, such as *hydrobenzamide*, $(\text{C}_6\text{H}_5\cdot\text{CH})_3\text{N}_2$, which is obtained when benzaldehyde is treated with ammonia.

Aromatic aldehydes of both types readily undergo *condensation* with many other fatty and aromatic compounds. When, for example, a mixture of benzaldehyde and acetone is treated with a few drops of caustic soda at ordinary temperatures, *benzylideneacetone*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CO}\cdot\text{CH}_3$ (m.p. 42°), is formed, and when benzaldehyde is warmed with aniline, it gives *benzylideneaniline*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{N}\cdot\text{C}_6\text{H}_5$ (m.p. 45°), a type of compound, which is known as a *Schiff's base*.

Nitrobenzaldehydes, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{CHO}$.—When treated with a mixture of nitric and sulphuric acids, benzaldehyde yields *m*-nitrobenzaldehyde (m.p. 58°) as principal product, small quantities of *o*-nitrobenzaldehyde (m.p. 41°) being formed at the same time.

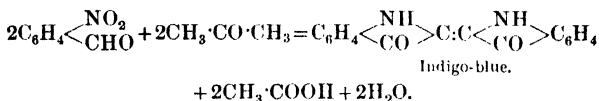
p-Nitrobenzaldehyde (m.p. 107°), and also the *o*-compound, are conveniently prepared by the oxidation of the corresponding nitrocinnamic acids (p. 464) with alkaline potassium permanganate,



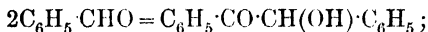
During the operation the mixture is shaken with benzene in order to extract the aldehyde as fast as it is formed, and thus prevent its further oxidation. The benzene solution is then evaporated, and the aldehydes are purified by recrystallisation.

The nitrobenzaldehydes are colourless, crystalline substances; when reduced with ferrous sulphate and ammonia, they are converted into the corresponding *aminobenzaldehydes*, $\text{C}_6\text{H}_4(\text{NH}_2)\cdot\text{CHO}$.

o-Nitrobenzaldehyde is a particularly interesting substance, as, when its solution in acetone is mixed with a few drops of dilute caustic soda, a precipitate of *indigo-blue* (*indigotin*) gradually forms (Baeyer),

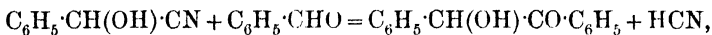


Benzoin, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CH}(\text{OH})\cdot\text{C}_6\text{H}_5$, a *ketonic alcohol*, is formed and separates in colourless crystals, when benzaldehyde (5 parts) is heated with a solution of potassium cyanide (1 part) in aqueous alcohol during about an hour, and the solution is then cooled,



it melts at 134° , and is oxidised by boiling concentrated nitric acid, giving a *diketone*, **benzil**, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CO}\cdot\text{C}_6\text{H}_5$, which is yellow and melts at 90° .

Many other aromatic (and certain aliphatic) aldehydes give products corresponding with benzoin when they are treated with potassium cyanide; this transformation, which is known as the *benzoin condensation*, depends on the intermediate formation of a hydroxy-cyanide (mandelonitrile),



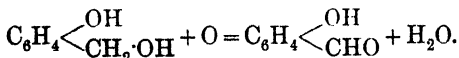
the necessary hydrogen cyanide being formed by the hydrolysis of the potassium cyanide.

Hydrobenzoin, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{CH}(\text{OH})\cdot\text{C}_6\text{H}_5$, is formed, together with benzyl alcohol by the reduction of benzaldehyde, just as a pinacol is formed from a ketone (p. 142); its molecule contains two structurally identical asymmetric carbon-groups, and like dihydroxysuccinic acid (tartaric acid) it exists in *d*-, *l*-, and *meso*-forms, also as a conglomerate.

Phenolic or Hydroxy-aldehydes.

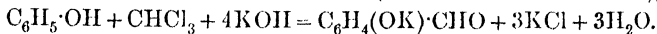
The hydroxy-derivatives of the aldehydes, such as the *hydroxy-benzaldehydes*, $\text{C}_6\text{H}_4(\text{OH})\cdot\text{CHO}$, which contain the hydroxyl-group united with the *nucleus*, combine the properties of phenols and aldehydes, and are classed as *phenolic aldehydes*.

They may be obtained by the oxidation of the corresponding phenolic alcohols; *saligenin* (p. 471), or *o-hydroxybenzyl alcohol*, for example, yields *salicylaldehyde* or *o-hydroxybenzaldehyde*,

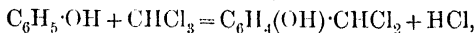


Such alcohols, however, are not easily obtained, and indeed in many cases have only been produced by the reduction of the phenolic aldehydes.

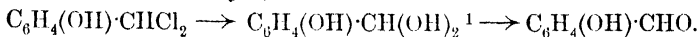
Many phenolic aldehydes may be prepared by heating phenols with chloroform in alkaline solution (Tiemann-Reimer reaction),



The changes which occur in this reaction are not understood; possibly the phenol reacts with the chloroform, in the presence of the alkali, yielding an intermediate product containing halogen,

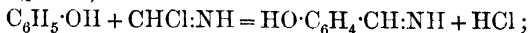


which, by the further action of the alkali, is converted into a hydroxybenzaldehyde, just as *benzalchloride*, $\text{C}_6\text{H}_5\cdot\text{CHCl}_2$, is transformed into *benzaldehyde*,



As a rule, the principal product is the *o*-hydroxyaldehyde, small quantities of the *p*-compound being produced at the same time.

Many phenolic aldehydes may also be prepared by treating phenols, dissolved in benzene or ether, with hydrogen cyanide and hydrogen chloride in the presence of anhydrous aluminium chloride (Gattermann; compare p. 439). Probably the two acids unite and form a compound, $\text{CHCl}:\text{NH}$, which then gives with the phenol an *aldimine* (p. 438),



this product is readily hydrolysed by acids or alkalis, with the formation of the *p*-hydroxy-aldehyde and ammonia.

Ethers of phenolic aldehydes may be obtained from phenolic ethers in a similar manner. When an alkyl cyanide is substituted for hydrogen cyanide, a phenol gives a ketone in the place of an aldehyde (Hoesch),



The phenolic aldehydes combine the properties of both phenols and aldehydes.

Salicylaldehyde, $\text{C}_6\text{H}_4(\text{OH})\cdot\text{CHO}$ (*o*-hydroxybenzaldehyde), may be obtained by oxidising saligenin with chromic acid (p. 471), but it is usually prepared from phenol by the Tiemann-Reimer reaction.

Phenol (25 grams) and caustic soda (80 grams) are dissolved in water (80 grams), the solution is heated to 65–70° in a flask provided with a reflux condenser, and chloroform (60 grams) is added in small quantities

¹ An intermediate product, $\text{C}_6\text{H}_4(\text{OH})\cdot\text{CH}(\text{OC}_6\text{H}_5)_2$, may also be formed.

at a time from a tap-funnel, cooling if necessary at first, and later heating, in order to keep the temperature constant. At the end of about two hours any unchanged chloroform is distilled off, and the alkaline solution is mixed with excess of dilute sulphuric acid and distilled in steam, when phenol and salicylaldehyde pass over. (The residue in the flask contains *p*-hydroxybenzaldehyde, which may be extracted from the filtered liquid with ether, and purified by recrystallisation.) The distillate is extracted with ether, the extract evaporated, and treated with two volumes of a strong solution of sodium bisulphite. The crystalline bisulphite compound of the aldehyde is filtered, using a suction-pump, and decomposed by heating it with dilute sulphuric acid; the regenerated *salicylaldehyde* is extracted with ether, dried over sodium sulphate, and purified by distillation.

Salicylaldehyde boils at 195° , and has a penetrating, aromatic odour; it dissolves readily in alkalis, giving yellow solutions, and its aqueous solution gives a violet colouration with ferric chloride. When reduced with sodium amalgam and water it yields *saligenin*, $C_6H_4(OH) \cdot CH_2 \cdot OH$ (p. 471), whereas oxidising agents convert it into *salicylic acid*, $C_6H_4(OH) \cdot COOH$.

p-Hydroxybenzaldehyde (m.p. 117°) dissolves readily in hot water, and gives, with ferric chloride, a slight violet colouration.

m-Hydroxybenzaldehyde is obtained by converting *m*-nitrobenzaldehyde into *m*-aminobenzaldehyde, and then displacing the amino-group by hydroxyl, with the aid of nitrous acid. It crystallises from water in needles, and melts at 104° .

Anisaldehyde, $C_6H_4(OCH_3) \cdot CHO$ (*p*-methoxybenzaldehyde), is prepared from oil of aniseed. This essential oil contains *anethole*, $C_6H_4(OCH_3) \cdot CH : CH \cdot CH_3$, a crystalline substance (m.p. 21°), which on oxidation with potassium dichromate and sulphuric acid is converted into *anisaldehyde*. It may be prepared synthetically by warming *p*-hydroxybenzaldehyde with alcoholic potash and methyl iodide (or dimethyl sulphate, p. 179),



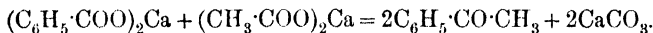
Anisaldehyde boils at 249° , and has a penetrating, aromatic odour; on reduction with sodium amalgam it yields *anisyl alcohol*, $C_6H_4(OCH_3) \cdot CH_2 \cdot OH$ (p. 472); on oxidation it gives *anisic acid*, $C_6H_4(OCH_3) \cdot COOH$ (p. 472).

Ketones.

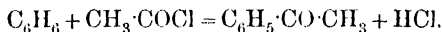
The ketones of the aromatic, like those of the aliphatic, series have the general formula, $R - CO - R'$, where R and R' represent

different or identical radicals, one of which, of course, must be aromatic.

Acetophenone, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CH}_3$ (phenylmethyl ketone, acetylbenzene), may be described as a typical aromatic ketone. It is formed, and distils over, when a mixture of calcium benzoate and calcium acetate is heated, a reaction which is exactly analogous to that by which mixed ketones of the aliphatic series are obtained,



It is most conveniently prepared by dropping acetyl chloride into well-cooled benzene, in the presence of anhydrous aluminium chloride,

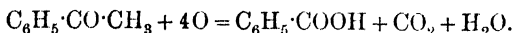


This method is a general one, as, by the use of other acid chlorides and other hydrocarbons, many other ketones may be prepared; it is an extension of Friedel and Crafts' method of preparing hydrocarbons (p. 361).

The benzene (15 parts, in c.c.) and aluminium chloride (7 parts) are placed in a flask fitted with a reflux condenser and cooled in ice. The acetyl chloride (5 parts, in c.c.) is added from a tap-funnel. When the evolution of hydrogen chloride ceases, the flask is taken out of the ice, and after about an hour's time the contents are *cautiously* added to crushed ice. The benzene solution is separated, washed with water and dilute alkali successively, dried with calcium chloride and submitted to distillation. The portion collected from about 196–204° should solidify at ordinary temperatures.

Acetophenone melts at 20·5°, and boils at 202°; it is used as a hypnotic in medicine, under the name of *Hyppnone*. Its chemical behaviour is so similar to that of the aliphatic ketones that most of its reactions, or at any rate those which are determined by the carbonyl-group, might be foretold from a consideration of those of acetone. On reduction with sodium amalgam and aqueous alcohol, acetophenone is converted into *phenylmethyl carbinol*, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{CH}_3$, just as acetone is transformed into isopropyl alcohol; like acetone, and other aliphatic ketones, it reacts with hydroxylamine, giving the *oxime*, $\text{C}_6\text{H}_5\cdot\text{C}(\text{:N}\cdot\text{OH})\cdot\text{CH}_3$ (m.p. 59°), and with phenylhydrazine, giving the *hydrazone*, $\text{C}_6\text{H}_5\cdot\text{C}(\text{:N}_2\text{HC}_6\text{H}_5)\cdot\text{CH}_3$ (m.p. 105°). It forms a cyanohydrin (hydroxycyanide), $\text{C}_6\text{H}_5\cdot\text{CMe}(\text{OH})\cdot\text{CN}$, with hydrogen cyanide, but does not combine with sodium hydrogen sulphite. On

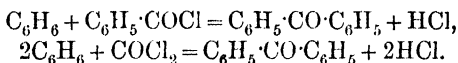
oxidation it is resolved into benzoic acid and carbon dioxide, just as acetone is oxidised to acetic acid and carbon dioxide,



Acetophenone shows also the general behaviour of aromatic compounds, inasmuch as it may be converted into nitro-, amino-, and halogen derivatives by the displacement of *nuclear* hydrogen.

The homologues of acetophenone, such as *propiophenone*, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{C}_2\text{H}_5$, *butyrophenone*, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{C}_3\text{H}_7$, &c., are of little importance, but *benzophenone*, an aromatic ketone of a different series, may be briefly described.

Benzophenone, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{C}_6\text{H}_5$ (diphenyl ketone or benzoyl-benzene), may be obtained by heating calcium benzoate, and by treating benzene with benzoyl chloride, or with carbonyl chloride, in the presence of aluminium chloride,

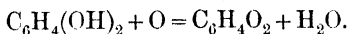


It melts at 46° , and, like aromatic ketones in general, does not combine with sodium hydrogen sulphite; when distilled over zinc-dust or reduced with amalgamated zinc and hydrochloric acid, it gives *diphenylmethane* (p. 370), just as acetophenone gives ethylbenzene.

Quinones.

When quinol (p. 432) is oxidised with an excess of ferric chloride in aqueous solution, a yellowish colouration is produced; the solution then darkens (p. 446), acquires a very penetrating odour, and, if sufficiently concentrated, deposits yellow crystals.

The substance formed in this way is named *quinone* (benzoquinone), and is the simplest member of a very interesting class of compounds; its formation may be expressed by the equation,



Quinone, $\text{C}_6\text{H}_4\text{O}_2$, is usually prepared by oxidising aniline with potassium dichromate and sulphuric acid.

Aniline (20 g.) is dissolved in water (500 c.c.) and sulphuric acid (87 c.c.), and finely powdered potassium dichromate (70 g.) is gradually added, the whole being cooled ($0-5^\circ$) and constantly stirred. When in the course of 2 hours one-third of the dichromate has been used, the mixture is left overnight, cooled again as before, and the rest of the dichromate gradually added. After the lapse of about eight hours, the crude quinone is separated by filtration, and purified by distillation in steam.

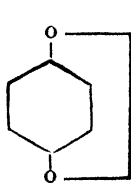
The reactions which occur during the oxidation of aniline to quinone are not understood, but aniline black, a very complex substance, is formed as an intermediate compound.

Quinone crystallises in golden-yellow prisms, melts at 116° , sublimes very readily, and is volatile in steam; it has a peculiar, irritating, and very characteristic smell, and is only sparingly soluble in water, but dissolves freely in many organic solvents. It is reduced by sulphurous acid giving quinol (p. 432).

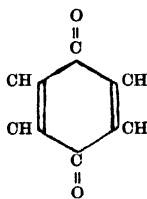
Quinhydrone, $C_6H_4O_2 \cdot C_6H_4(OH)_2$, a dark green, crystalline additive compound of quinone and quinol, is formed as an intermediate product in this reaction, and also during the oxidation of quinol to quinone with ferric chloride (p. 445).

Constitution of Quinone.—It is known that the two oxygen atoms in the molecule of quinone are in the *para*-position to one another because when quinone is reduced, it gives *quinol* (*para*-dihydroxybenzene), from which it is produced by oxidation (see above); further, when quinone is treated with phosphorus pentachloride, it is converted into *para*-dichlorobenzene. From these facts it would also seem that each of the oxygen atoms is combined with a carbon atom by one bond only, and that the structure of quinone must be expressed by the formula I. (below). But in some respects quinone behaves as if its molecule contained two $>C=O$ groups, each having properties similar to those of the carbonyl-groups in compounds such as acetone, acetophenone, &c.; when treated with a solution of a hydroxylamine salt, for example, quinone yields a *monoxime*, $C_6H_4 \begin{smallmatrix} \diagup O \\ \diagdown N \cdot OH \end{smallmatrix}$ (*p*-nitrosophenol, p. 397),¹

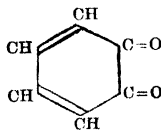
and also a *dioxime*, $C_6H_4 \begin{smallmatrix} \diagup N \cdot OH \\ \diagdown N \cdot OH \end{smallmatrix}$.



I.



II.



III.

¹ Quinone monoxime and *p*-nitrosophenol are tautomeric (p. 183).

If, from this evidence, it were concluded that quinone is a diketone, then its structure must be expressed by the formula II. which is fundamentally different from that of any aromatic compound so far described, because the closed-chain of six carbon atoms, here shown, does not represent a benzene nucleus, but contains two pairs of *unsaturated* carbon atoms, united together in the same way as those in the molecules of olefinic compounds. This view is strongly supported by the fact that quinone combines *directly* with bromine, at ordinary temperatures, in the absence of direct sunlight, giving a di- and a tetra-bromide, $C_6H_4Br_2O_2$ and $C_6H_4Br_4O_2$, whereas aromatic (benzenoid) compounds as a class do *not* form such additive products. The constitution of quinone, therefore, is represented by formula II.¹; the compound is *not* aromatic, but is a diketone derived from a cyclic *di-olefine* and its formation from, and conversion into, quinol, as well as its transformation into *p*-dichlorobenzene involve unknown stages.

Benzoquinone and many other *para*-quinones (that is to say, quinones in which the two carbonyl-groups are in the *para*-position to one another) may be produced by the oxidation, with chromic acid or ferric chloride, of many hydroxy- and amino-compounds, which contain these substituent groups in the *para*-position; quinone, for example, is formed not only from aniline and quinol, but also by oxidising *p*-aminophenol, $C_6H_4(OH) \cdot NH_2$, and *p*-phenylenediamine, $C_6H_4(NH_2)_2$, and *p*-toluquinone, $[O:O:CH_3 = 1:4:2]$, is obtained in a similar manner by the oxidation of *p*-toluylenediamine, $C_6H_4(NH_2)_2 \cdot CH_3$, $[NH_2:NH_2:CH_3 = 1:4:2]$, as well as from *o*-toluidine. All *para*-quinones resemble (benzo-) quinone in smell, in having a yellow colour, and in being readily volatile (compare p. 487).

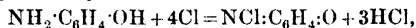
o-Benzoquinone, $C_6H_4O_2$ (formula III.),¹ is a light-red, crystalline substance, which is obtained when catechol is oxidised with silver oxide in dry ethereal solution (in the presence of anhydrous sodium sulphate). It has no smell, is not volatile in steam, and decomposes when it is heated at 60–70°; it is reduced to catechol by sulphurous acid in aqueous solution.

m-Quinones are not known (and apparently cannot exist); this fact affords further evidence in favour of the formulæ given to

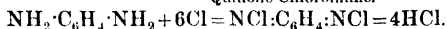
¹The symbols and double bonds should be shown, as here, in writing the structural formulæ of these quinones.

the **o**- and **p**-compounds, because a corresponding formula for a **m**-quinone cannot be written.

When bleaching-powder is used in oxidising amino-compounds, such as the above, *quinone chloroimines* and *quinone dichlorodimines* are formed in the place of quinones,



Quinone Chloroimine.



Quinone Dichlorodimine.

The quinone chloroimines and dichlorodimines resemble quinone in many respects; they are crystalline, readily volatile in steam, and are respectively converted into **p** aminophenol and **p**-phenylenediamine, or their derivatives, on reduction.

Chloranil, $\text{O} \cdot \text{C}_6\text{Cl}_4 \cdot \text{O}$ (tetrachloroquinone), is produced by treating phenol with hydrochloric acid and potassium chlorate, oxidation and chlorination taking place; it crystallises in yellow plates, sublimes without melting, and is sparingly soluble in alcohol, and nearly insoluble in water. It is readily reduced to *tetrachloroquinol*, $\text{HO} \cdot \text{C}_6\text{Cl}_4 \cdot \text{OH}$, and is sometimes used as an oxidising agent in the preparation of dyes, when the use of inorganic oxidising agents is undesirable.

CHAPTER XXXI.

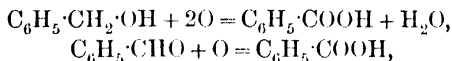
CARBOXYLIC ACIDS.

THE carboxylic acids of the aromatic series are derived from the aromatic hydrocarbons, just as those of the aliphatic series are derived from the paraffins—namely, by the substitution of one or more carboxyl-groups for a corresponding number of hydrogen atoms. In this, as in other cases, however, one of two classes of compounds may be obtained, according as substitution takes place in the *nucleus* or in the *side-chain*; benzene, of course, yields only acids of the first class, such as *benzoic acid*, $\text{C}_6\text{H}_5 \cdot \text{COOH}$, the three (**o.m.p.**) *phthalic acids*, $\text{C}_6\text{H}_4(\text{COOH})_2$, the three tricarboxylic acids, $\text{C}_6\text{H}_3(\text{COOH})_3$, &c., but toluene (and all the higher homologues) may give rise to derivatives of both kinds—as, for example, the three *toluic acids*, $\text{C}_6\text{H}_4(\text{CH}_3) \cdot \text{COOH}$, and *phenylacetic acid*, $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{COOH}$.

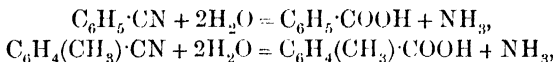
Although there are no very important differences in the properties of these two classes of acids, it is more convenient

to describe them separately, taking first those compounds in which the carboxyl-groups are directly united with carbon of the *nucleus*.

Preparation.—Such acids may be obtained by oxidising the alcohols or aldehydes,



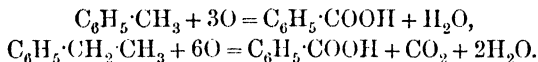
and by hydrolysing the nitriles (p. 454) with alkalis or mineral acids,



reactions which are exactly similar to those employed in the case of the fatty acids (p. 167).

Aromatic acids may also be obtained by treating aryl Grignard reagents (p. 380) with dry carbon dioxide, and then decomposing the products with a mineral acid (p. 209).

Perhaps, however, the most important method, and one which has no counterpart in the aliphatic series, consists in oxidising the homologues of benzene with dilute nitric acid, chromic acid, or potassium permanganate,

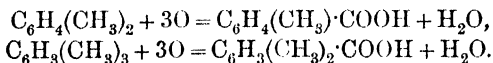


As a rule, only those acids which contain the carboxyl-group united with carbon of the *nucleus* can be obtained in this way, because a saturated side-chain is oxidised to $-\text{COOH}$, no matter how many $-\text{CH}_2-$ groups it may contain; in other words, all homologues of benzene which contain only one alkyl-group yield *benzoic acid*, whereas those containing two, give one of the *phthalic acids*.

The reason for this is that when the side-chain contains more than one carbon atom, the $-\text{CH}_2-$ group, which is united to carbon of the nucleus, is attacked before the terminal $-\text{CH}_3$ group, and the intermediate product, a ketone, then undergoes further oxidation in the usual way. When, however, the side-chain is unsaturated, it may be possible to restrict oxidation to the $-\text{CH}:\text{CH}-$ group; from *phenylbutylene*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}:\text{CH}_2$ (p. 478), for example, phenylpropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$ (p. 462) might be obtained.

When two or more side-chains are present, one may be oxidised

before the other is attacked, in which case an alkyl-substituted acid is obtained (compare mesitylenic acid, p. 345),

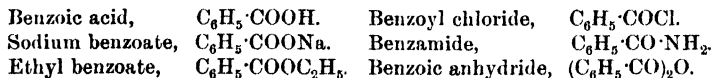


Oxidation is frequently carried out by boiling the hydrocarbon with nitric acid (1 vol.), diluted with water (2-4 vols.), until brown fumes are no longer formed. The mixture is then made slightly alkaline, and any unchanged hydrocarbon and traces of nitrohydrocarbon are separated by distillation with steam, or by extraction with ether; the solution is then strongly acidified, and the precipitated acid purified by recrystallisation.

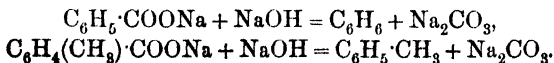
Most hydrocarbons are only very slowly attacked by oxidising agents, and therefore it is often advantageous first to substitute chlorine or a hydroxy-group for hydrogen of the side-chain, as in this way oxidation is facilitated. *Benzyl chloride*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\text{Cl}$, and *benzyl acetate*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{O}\cdot\text{CO}\cdot\text{CH}_3$ (p. 436), for example, are much more readily oxidised than toluene, because they undergo hydrolysis, giving benzyl alcohol, which is then rapidly attacked.

Ordinary coal is oxidised by an alkaline solution of potassium permanganate giving nearly 50 per cent. of a complex mixture of benzenecarboxylic acids; ten of the twelve theoretically possible acids are thus obtained, the missing compounds being benzoic acid and one of the tetracarboxylic acids, $\text{C}_6\text{H}_2(\text{COOH})_4$. The hexacarboxylic acid, $\text{C}_6(\text{COOH})_6$ (p. 460), is also formed when graphite is oxidised with fuming nitric acid.

Properties.—The monocarboxylic acids are crystalline, and generally distil without decomposing; they are sparingly soluble in cold water, but dissolve much more readily in hot water and organic solvents. As regards all those properties which are determined by the carboxyl-group, the aromatic acids are closely analogous to the aliphatic compounds, and give corresponding derivatives, as the following examples show:

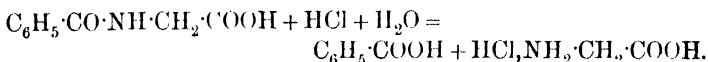


When heated with soda-lime, they are decomposed with loss of carbon dioxide and formation of the corresponding hydrocarbons, just as acetic acid under similar circumstances yields methane,

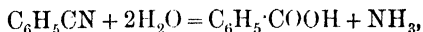


Benzoic acid, $C_6H_5 \cdot COOH$, occurs in the free state in many resins, especially in gum benzoin and Peru balsam; it is also found in the urine of the ox and the horse (about 2 per cent.), as *hippuric acid* or *benzoylglycine*, $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot COOH$, a crystalline compound melting at 187° .

It may be obtained by heating gum benzoin and recrystallising the crude sublimate from water; or by boiling hippuric acid with concentrated hydrochloric acid during about an hour, and then cooling the solution,

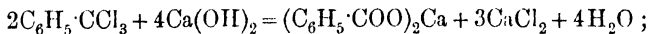


It may also be prepared by oxidising toluene, benzyl alcohol, or benzaldehyde, by hydrolysing *benzonitrile* (p. 453) with acids or alkalis,



and by treating benzaldehyde with caustic potash or soda (Cannizzaro reaction, p. 440).

Benzoic acid is manufactured by hydrolysing crude benzo-trichloride as already described (p. 438),



the benzoic acid is precipitated from the solution of its calcium salt with hydrochloric acid and recrystallised or distilled.

Benzoic acid separates from water in glistening crystals, melts at 120.5° , and boils at 249° , but it sublimes very readily even at 100° , and is volatile in steam; it dissolves in 400 parts of water at 15° , but is readily soluble in hot water and many organic solvents. Its vapour has a characteristic odour (which may serve for the identification of the acid), and an irritating action on the throat, causing violent coughing. Most of the metallic salts of benzoic acid are soluble in water, and crystallise well, but the *silver* salt is only very sparingly soluble in the cold.

Ethyl benzoate, $C_6H_5 \cdot COOC_2H_5$, is prepared by saturating a solution of benzoic acid (1 part) in alcohol (3 parts) with hydrogen chloride, and then warming the solution (with reflux condenser) during about two hours (compare p. 171).

The excess of alcohol is then separated by distillation, and the oily residue is shaken with a dilute solution of sodium carbonate until free from acids; the ester is washed with water, dried with calcium

chloride, and distilled. A little ether may be used to dissolve the ester, if it does not separate well from the aqueous washings.

It boils at 213° , has a pleasant aromatic odour, and is readily hydrolysed by boiling alkalis.

Methyl benzoate boils at 199° .

Phenyl benzoate, $C_6H_5 \cdot CO \cdot OC_6H_5$, prepared by treating phenol with benzoyl chloride (below), melts at 71° , and is readily hydrolysed by aqueous alkalis.

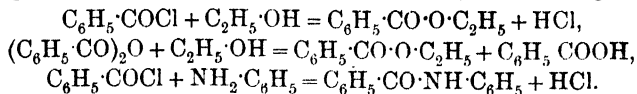
Benzoyl chloride, $C_6H_5 \cdot COCl$, is easily obtained by treating benzoic acid with phosphorus pentachloride.

The dry acid is placed in a distillation flask, and about 5 per cent. more than one molecular proportion of the pentachloride is added. When the reaction is finished, the mixture of phosphorus oxychloride (b.p. 107°) and benzoyl chloride is submitted to fractional distillation. The whole operation is conducted in a fume-cupboard.

It is a colourless oil, has a most irritating odour, and boils at 198° ; it is gradually decomposed by water, yielding benzoic acid and hydrochloric acid. Benzoyl chloride is a very important laboratory reagent (see below).

Benzoic anhydride, $(C_6H_5 \cdot CO)_2O$, is produced when benzoyl chloride is treated with sodium benzoate, just as acetic anhydride is formed by the interaction of acetyl chloride and sodium acetate (p. 161); it melts at 42° , and closely resembles acetic anhydride in ordinary chemical properties, but it reacts only very slowly with cold water or sodium carbonate solution.

Benzoyl chloride and benzoic anhydride, more especially the former, are frequently used for the *benzoylation* of hydroxy- and amino-compounds, as they react with such substances, yielding *benzoyl-derivatives*, the univalent *benzoyl-group*, $C_6H_5 \cdot CO-$, taking the place of the hydrogen atom of the hydroxyl- or amino-group,



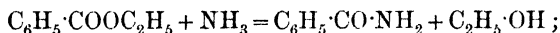
As such benzoyl-derivatives usually crystallise much more readily than the corresponding acetyl-derivatives, they are generally prepared in preference to the latter when it is a question of the identification or isolation of a substance.

Benzoyl-derivatives may be prepared by heating the hydroxy- or amino-compound with benzoyl chloride alone, or in the presence of pyridine (p. 505), which combines with the hydrogen chloride formed in

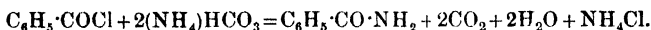
the reaction. On a small scale, however, the *Schotten-Baumann* method may be used: Benzoyl chloride and 10 per cent. caustic alkali are added alternately, in *small* quantities at a time, to the compound, which is either dissolved or suspended in water, and, after each addition, the mixture is well shaken and cooled. The addition is continued until no further formation of the benzoyl-derivative seems to occur. Alkali alone is then added until the disagreeable smell of benzoyl chloride is no longer noticed, and the solution remains permanently *alkaline*; unless this is done, benzoic acid separates in crystals, and renders the benzoyl-derivative impure. The product is finally separated by filtration or by extraction with ether, and purified in a suitable manner. The alkali serves to convert phenols into their more reactive metallic derivatives, to prevent the formation of the less reactive salts of the bases, and also to dissolve the benzoic acid which is produced during benzoylation.

p-Nitrobenzoyl chloride (m.p. 75°) is also frequently used in a similar manner, as the *p*-nitrobenzoyl-derivatives of bases, &c. usually crystallise well.

Benzamide, $C_6H_5 \cdot CO \cdot NH_2$, may be taken as an example of an aromatic amide; it may be obtained by reactions similar to those employed in the case of acetamide (p. 162), as, for example, by shaking ethyl benzoate with concentrated ammonia,

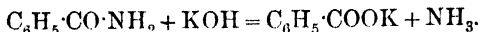


but it is also conveniently prepared by treating benzoyl chloride with excess of dry 'ammonium carbonate,'

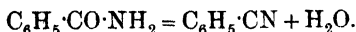


The ammonium carbonate (about 10 g.) is placed in a mortar, the benzoyl chloride (4–5 g.) is added, and the two substances are well mixed with a pestle; if there is still a strong smell of the chloride at the end of about ten minutes, a little more ammonium carbonate is stirred in. The solid is extracted with a little cold water, which removes the ammonium salts, and is then recrystallised from boiling water.

Benzamide melts at 128°, and is sparingly soluble in cold, but readily soluble in hot, water; like other amides, it is decomposed by boiling alkalis, yielding ammonia and an alkali salt,

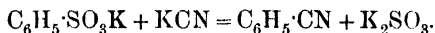


Benzonitrile, $C_6H_5 \cdot CN$ (phenyl cyanide), may be obtained by heating benzamide with phosphorus pentoxide, a method similar to that employed in the preparation of aliphatic nitriles,

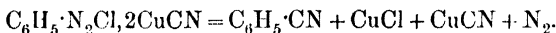


It cannot be prepared by treating chloro- or bromo-benzene with

potassium cyanide, because the halogen atom is so firmly held that no interaction occurs, but it may be obtained by fusing potassium benzenesulphonate with potassium cyanide (or with potassium ferrocyanide, which yields the cyanide, p. 312),



It is most conveniently prepared from aniline by Sandmeyer's reaction—namely, by treating a solution of phenyldiazonium chloride with potassium cuprous cyanide,



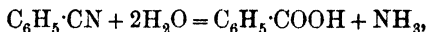
Aniline (1 part) is *diazotised* exactly as already described (p. 403), and the solution of the diazonium chloride is then gradually added to a hot solution of potassium cuprous cyanide; the product is distilled in steam and extracted with ether. The extract is washed with dilute caustic soda, and dried with calcium chloride; the ether is then distilled, and the cyanide is purified by distillation.

The solution of potassium cuprous cyanide required above is prepared by slowly adding powdered potassium cyanide (3 parts) to a hot solution of hydrated cupric sulphate ($2\frac{1}{2}$ parts) in water (15 parts),

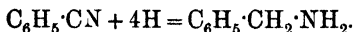


This and the subsequent operations, including steam distillation, must be conducted in a good draught cupboard, on account of the evolution of cyanogen and hydrogen cyanide, both of which are *highly poisonous* (pp. 309, 311).

Benzonitrile boils at 191° , and smells rather like nitrobenzene. Its reactions resemble those of the aliphatic nitriles; thus, it is converted into the corresponding acid on hydrolysis with alkalis (or mineral acids),



and into a primary amine on reduction,



Other aromatic nitriles, such as the three *tolunitriles*, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{CN}$, are known; also compounds such as *phenyl-acetonitrile* (*benzyl cyanide*, p. 462), $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CN}$, which contain the cyanogen-group in the side-chain.

Substitution Products of Benzoic Acid.—Benzoic acid is attacked by chlorine, bromine, nitric acid, and sulphuric acid, giving a *meta*-derivative in all cases, according to rule (p. 382); when, for example, benzoic acid is heated with bromine and water at 125° , *m*-bromobenzoic acid, $\text{C}_6\text{H}_4\text{Br}\cdot\text{COOH}$ (m.p. 155°), is formed.

The *o*- and *p*-*bromobenzoic acids* are obtained by oxidising the corresponding *bromotoluenes* with dilute nitric or chromic acid; the former melts at 147°, the latter at 254°. Nitric acid, in the presence of sulphuric acid, acts readily on benzoic acid, *m*-*nitrobenzoic acid*, $C_6H_4(NO_2) \cdot COOH$ (m.p. 141°), being the principal product; *o*-*nitrobenzoic acid* (m.p. 147°) and *p*-*nitrobenzoic acid* (m.p. 240°) are obtained by the oxidation of *o*- and *p*-*nitrotoluene* respectively (p. 385); when these acids are reduced with tin and hydrochloric acid, they yield the corresponding *aminobenzoic acids*, $C_6H_4(NH_2) \cdot COOH$, which, like glycine (p. 202), form salts with mineral acids and with bases.

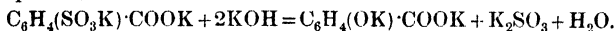
Anthranilic acid, $C_6H_4(NH_2) \cdot COOH$ (*o*-aminobenzoic acid), was first obtained by the oxidation of indigo (p. 606); it is prepared by treating phthalimide (p. 458) with sodium hydroxide and sodium hypochlorite,

$$C_6H_4 \begin{smallmatrix} \text{CO} \\ \text{CO} \end{smallmatrix} \text{NH} + NaOCl + 3NaOH = C_6H_4 \begin{smallmatrix} NH_2 \\ \text{COONa} \end{smallmatrix} + Na_2CO_3 + NaCl + H_2O,$$

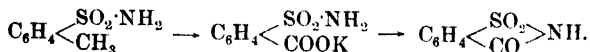
and is an intermediate product in the manufacture of indigo (p. 607). It melts at 144°, decomposes at higher temperatures, giving aniline and carbon dioxide, and is sparingly soluble in water.

When heated with sulphuric acid, benzoic acid is converted into *m*-*sulphobenzoic acid*, $C_6H_4(SO_3H) \cdot COOH$, small quantities of the *p*-acid also being produced. The *o*- and *p*-acids are obtained by oxidising the corresponding *toluenesulphonic acids* (p. 418).

The sulphobenzoic acids are very soluble in water; when fused with potash they yield phenolic acids (p. 467), just as benzenesulphonic acid gives phenol,

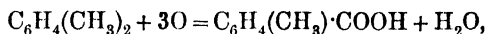


Saccharin, $C_6H_4 \begin{smallmatrix} SO_2 \\ \text{CO} \end{smallmatrix} \text{NH}$, is the *imide* of *o*-sulphobenzoic acid, and is remarkable for having the sweetening effect of about 400 times its weight of sucrose. It is prepared from toluene, which is first treated with chlorosulphonic acid (p. 416); the resulting *o*-toluenesulphonyl chloride is partially freed from the *p*-compound by freezing out the latter, and converted into its *amide* with ammonia. The purified amide is oxidised with alkaline potassium permanganate and the product is treated with acid in order to decompose the potassium salt; the free acid then loses water yielding saccharin (m.p. 220°),



The ammonium salt of the imide, *sucramine*, is soluble in water and has an even greater sweetening power than saccharin.

The three (**o.m.p.**) **toluic acids**, $\text{C}_6\text{H}_4(\text{CH}_3)\cdot\text{COOH}$, may be produced by oxidising the respective *xylenes* with dilute nitric acid,



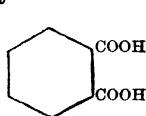
but the **o**- and **p**-acids are best prepared by converting the corresponding *toluidines* into the nitriles by Sandmeyer's reaction (p. 402), and then hydrolysing the latter with acids or alkalis,



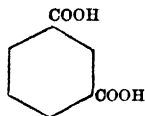
The **o**-, **m**-, and **p**-toluic acids melt at 107° , 112° , and 181° respectively, and resemble benzoic acid very closely, but since they contain a methyl-group, they have also properties which are not shown by benzoic acid; on oxidation, for example, they are converted into the corresponding *phthalic acids*, just as toluene is transformed into benzoic acid.

Dicarboxylic Acids.

The important dicarboxylic acids are the three (**o.m.p.**) *phthalic acids*, or benzenedicarboxylic acids, which are respectively represented by the formulæ,



Phthalic Acid.

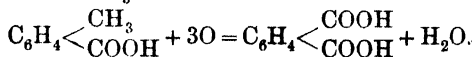
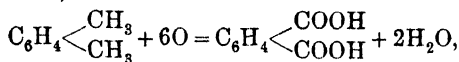


Isophthalic Acid.



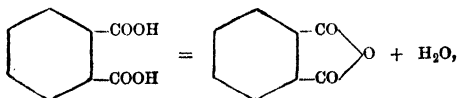
Terephthalic Acid.

These compounds may be prepared by the oxidation of the corresponding *xylenes* (dimethylbenzenes) with dilute nitric acid, or by treating the *toluic acids* with potassium permanganate in alkaline solution,



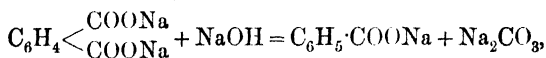
They are colourless, crystalline substances, and have the properties of aliphatic dicarboxylic acids. They yield normal and hydrogen metallic salts and esters, acid chlorides, amides, &c., which are formed by reactions similar to those employed in the preparation of corresponding derivatives of dicarboxylic acids of the aliphatic series.

Phthalic acid, like succinic acid (p. 247), is converted into its anhydride when it is strongly heated,



but an anhydride of *isophthalic acid* or of *terephthalic acid* cannot be produced; it is, in fact, a general rule that the formation of an anhydride from *one* molecule of an acid (an *inner* anhydride) takes place only when the two carboxyl groups combined with the *benzene nucleus* are in the *o*-position, never when they occupy the *m*- or *p*-position (compare p. 345).

When cautiously heated with soda-lime, all these dicarboxylic acids yield benzoic acid,



but at high temperatures both carboxyl-groups are displaced by hydrogen, and benzene is formed.

When phthalic acid is strongly heated with about twice its weight of resorcinol, *fluorescein* (p. 592) is produced, and the reddish-brown product, when dissolved in caustic soda and poured into a large quantity of water, yields a solution having a green fluorescence. This reaction is shown by all the *o*-dicarboxylic acids of the benzene series, but not by the *m*- and *p*-dicarboxylic acids; it is also shown by acids of the aliphatic series, such as succinic acid, which give inner anhydrides, and may therefore be used for the identification of such compounds. When the anhydride of the dicarboxylic acid, unlike that of phthalic acid, is not readily formed, a drop of sulphuric acid is added before the mixture is heated.

Phthalic acid, $\text{C}_6\text{H}_4(\text{COOH})_2$ (benzene-*o*-dicarboxylic acid), may be obtained by oxidising *o*-xylene or *o*-toluic acid; it used to be manufactured by oxidising *naphthalene* (p. 476) with sulphuric acid, in the presence of mercuric sulphate:

Naphthalene dissolves in hot concentrated (or fuming) sulphuric acid, giving sulphonic acids. At about 295–300°, in the presence of about 3 per cent. of mercuric sulphate, these acids are rapidly oxidised, sulphur dioxide is evolved, and phthalic anhydride sublimes or distils. The crude anhydride is separated, washed with water, dried and sublimed.

In the laboratory, naphthalene (1 part), concentrated sulphuric acid (8 parts), and mercuric sulphate (0.1 part) are gradually heated together in a retort until most of the contents (except the mercuric salt) have distilled. The anhydride is separated, washed with water, and dissolved in boiling caustic soda; from the filtered solution phthalic acid is precipitated on the addition of sulphuric acid.

The acid is now obtained from its anhydride, which is manufactured by the atmospheric oxidation of naphthalene, at about 330° , in the presence of vanadium pentoxide.

Phthalic acid crystallises in prisms, and melts from about 184° , with the formation of the anhydride, so that, when the melted substance has solidified, and the melting-point is again determined, it is found to be about 128° (that of the anhydride).

Phthalic acid dissolves in about 100 parts of water at ordinary temperatures; it is readily soluble in many organic liquids. The barium salt, $C_6H_4(COO)_2Ba$, precipitated on the addition of barium chloride to a neutral solution of the ammonium salt, is very sparingly soluble in water.

Ethyl phthalate, $C_6H_4(COOC_2H_5)_2$, is readily prepared by saturating an alcoholic solution of phthalic acid (or its anhydride) with hydrogen chloride. It is a liquid (b.p. 288°).

Phthalyl chloride, $C_6H_4(COCl)_2$, is prepared by heating phthalic anhydride (1 mol.) with phosphorus pentachloride (1 mol.). It is a colourless oil, boils at 275° (726 mm.), and is slowly decomposed by water, with regeneration of phthalic acid. In many of its reactions it behaves as if it had the constitution represented by the formula, $C_6H_4<\begin{smallmatrix} CCl_2 \\ CO \end{smallmatrix}>O$ (compare succinyl chloride, p. 248).

Phthalic anhydride, $C_6H_4<\begin{smallmatrix} CO \\ CO \end{smallmatrix}>O$, is produced when phthalic acid is heated at about 200° . It sublimes readily in long needles, melting at 128° ; it does not dissolve immediately in a cold solution of sodium carbonate, but is readily hydrolysed by alkalis. It is used in the manufacture of *glyptal* plastics and dyes.

Phthalimide, $C_6H_4<\begin{smallmatrix} CO \\ CO \end{smallmatrix}>NH$, may be prepared by heating an intimate mixture of phthalic anhydride (5 parts) and dry ammonium carbonate (6 parts).

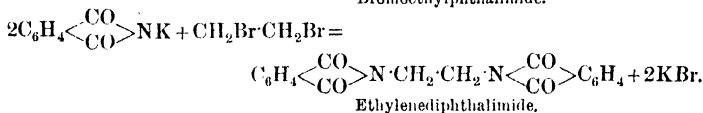
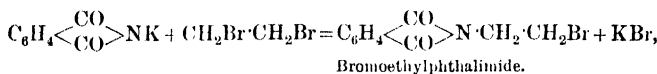
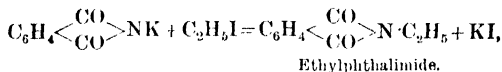
The mixture is heated in a small flask over a wire gauze; it first becomes pasty and then gradually hard again in the course of about

15 minutes. The product is recrystallised from boiling water or aqueous alcohol.

It melts at 238° and is an intermediate product in the synthesis of indigo from naphthalene (p. 607).

Phthalimide, like succinimide (p. 248), yields a potassium derivative, $C_6H_4<\begin{smallmatrix} CO \\ CO \end{smallmatrix}>NK$, with alcoholic potash, and this compound, as was shown by Gabriel, is very useful in the preparation of primary amines and their derivatives (p. 543).

Potassium phthalimide, or a mixture of the imide and dry potassium carbonate, reacts with alkyl halides, aliphatic di-halides, such as ethylene dibromide, etc., giving substituted phthalimides,



These products are decomposed by mineral acids and by alkalis (most readily by hydrazine), giving an amine, or a bromo- or hydroxy-amine; *ethylphthalimide*, for example, gives ethylamine, whereas *bromoethylphthalimide* gives *bromoethylamine*, $NH_2 \cdot CH_2 \cdot CH_2Br$, or *aminoethyl alcohol*, $NH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, according to the reagent used. *Ethylenediphtalimide* yields *ethylenediamine*, $NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$.

Isophthalic acid, $C_6H_4(COOH)_2$ (benzene-*m*-dicarboxylic acid), is produced by oxidising *m-xylene* with nitric acid or chromic acid; or from *m-toluic acid* (p. 456), by oxidation with potassium permanganate in alkaline solution.

It crystallises in needles, melts above 300°, and when strongly heated sublimes unchanged; it is very sparingly soluble in water. *Methyl isophthalate*, $C_6H_4(COOCH_3)_2$, melts at 65°.

Terephthalic acid, $C_6H_4(COOH)_2$ (benzene-*p*-dicarboxylic acid), is formed by the oxidation of *p-xylene*, *p-toluic acid*, and of all di-alkyl substitution derivatives of benzene, which, like *cymene*, $CH_3 \cdot C_6H_4 \cdot CH(CH_3)_2$, contain the alkyl-groups in the *p*-position. It is best prepared by oxidising *p-toluic acid* (p. 456) in alkaline solution with potassium permanganate.

Terephthalic acid is almost insoluble in water, and, when heated, sublimes without melting; the *methyl* ester, $C_6H_4(COOCH_3)_2$, melts at 140° .

Isophthalic acid, terephthalic acid, and other acids which have an indefinite melting-point, or which melt above 300° , are best identified with the aid of their methyl esters, which generally crystallise well, and melt at comparatively low temperatures.

To identify it, the acid (0.1–0.5 g.) is warmed in a test-tube with about three times its weight of phosphorus pentachloride, and the clear solution, which now contains the chloride of the acid, is poured into excess of methyl alcohol. As soon as the vigorous reaction has subsided, the liquid is diluted with water, and the crude methyl ester is collected and recrystallised; its melting-point is then determined.

Benzenhexacarboxylic acid, $C_6(COOH)_6$, as already mentioned (p. 450), is formed by the oxidation of graphite or of coal. Its *aluminium* salt, $C_6(COO)_6Al_3 \cdot 18H_2O$, occurs naturally in crystals in certain beds of brown-coal, or lignite, and from its appearance was called *honey-stone*; the acid isolated from this salt was named *mellitic acid* (lat. *mel*, honey), and was afterwards obtained by oxidising *hexamethylbenzene*, $C_6(CH_3)_6$, with potassium permanganate. The acid crystallises in lustrous needles, is readily soluble in water, decomposes when it is heated, and gives benzene when its sodium salt is distilled with soda-lime.

Phenylacetic Acid, Phenylpropionic Acid, and their Derivatives.

Many aromatic compounds already described have been shown to have certain properties similar to those of members of the aliphatic series, and it has been pointed out that this is due to the presence, in the former, of groups of atoms (*side-chains*), which have an aliphatic structure; benzyl chloride, for example, has many properties in common with methyl chloride, benzyl alcohol with methyl alcohol, benzylamine with methylamine, and so on, because similar groups or radicals confer, as a rule, similar properties on the compounds in which they occur. Since, moreover, nearly all aliphatic compounds may theoretically be converted into aromatic compounds of corresponding types, by the substitution of a phenyl-group for hydrogen, it follows that any series of aliphatic compounds may have its counterpart in the aromatic group. This is well illustrated in the case of the carboxylic

acids; corresponding with the aliphatic, there is a series of aromatic acids, which may be regarded as derived from the former in the manner just mentioned.

Formic acid, $\text{H}\cdot\text{COOH}$,

Benzoic acid, $\text{C}_6\text{H}_5\cdot\text{COOH}$ (phenylformic acid).

Acetic acid, $\text{CH}_3\cdot\text{COOH}$,

Phenylacetic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{COOH}$.

Propionic acid, $\text{CH}_3\cdot\text{CH}_2\cdot\text{COOH}$,

Phenylpropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$.

Butyric acid, $\text{CH}_3\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$,

Phenylbutyric acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$.

With the exception of benzoic acid, the above aromatic acids are derived from the aromatic hydrocarbons by the substitution of carboxyl for hydrogen of the *side-chains*. They have not only the characteristic properties of aromatic compounds in general, but also those of aliphatic acids, and, like the latter, they may be converted, in many cases, into unsaturated compounds by the loss of two or more atoms of hydrogen; the compounds thus produced correspond with the unsaturated aliphatic acids, as the following examples will show:

Propionic acid, $\text{CH}_3\cdot\text{CH}_2\cdot\text{COOH}$,

Phenylpropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$.

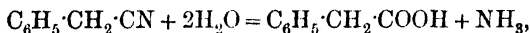
Acrylic acid, $\text{CH}_2\cdot\text{CH}\cdot\text{COOH}$,

Phenylacrylic acid, $\text{C}_6\text{H}_5\cdot\text{CH}\cdot\text{CH}\cdot\text{COOH}$.

Propiolic acid, $\text{CH}\cdot\text{C}\cdot\text{COOH}$,

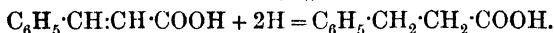
Phenylpropiolic acid, $\text{C}_6\text{H}_5\cdot\text{C}\cdot\text{C}\cdot\text{COOH}$.

Preparation.—Aromatic acids, containing the carboxyl-group in the *side-chain*, may be prepared by *carefully* oxidising the corresponding alcohols and aldehydes, and by hydrolysing the corresponding nitriles with alkalis or mineral acids,



but these methods are limited in application, owing to the difficulty of obtaining the requisite substances.

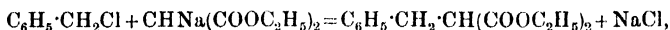
The more important general methods are: (1) By the reduction of the corresponding unsaturated acids, many of which are prepared without much difficulty (p. 463),



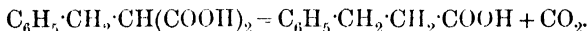
(2) By the interaction of the sodium compound of ethyl malonate or of ethyl acetoacetate and a halogen derivative of an aromatic hydrocarbon. As, in this method, the procedure is exactly

similar to that employed in preparing aliphatic acids (pp. 183-184), one example only need be given—namely, the synthesis of *phenylpropionic acid*.

The sodium compound of ethyl malonate is heated with benzyl chloride, and the *ethyl benzylmalonate* which is thus produced,

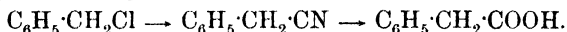


is hydrolysed with alcoholic potash. The *benzylmalonic acid* is then isolated, and heated at 200° , when it is converted into *phenylpropionic acid*, with the loss of carbon dioxide,



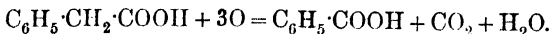
It should be remembered that *only* those halogen derivatives in which the halogen is in the *side-chain* can be employed in such syntheses, because when the halogen is united with the nucleus, as in *monochlorotoluene*, $\text{C}_6\text{H}_4\text{Cl}\cdot\text{CH}_3$, for example, no action takes place (compare p. 374).

Phenylacetic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{COOH}$, is prepared by boiling an alcoholic solution of benzyl chloride with potassium cyanide during about three hours; the *benzyl cyanide* (b.p. 232°), which is thus formed, is isolated by fractional distillation and hydrolysed with boiling diluted sulphuric acid,



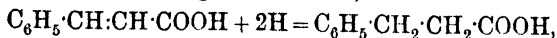
Phenylacetic acid melts at 76.5° , boils at 265° , and crystallises from water in glistening plates; it has a characteristic smell, and forms many derivatives just as do benzoic and acetic acids.

When oxidised with chromic acid it yields benzoic acid, a change very different from that undergone by the isomeric toluic acids (p. 456),



Phenylethyl alcohol, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{OH}$ (b.p. 219°), prepared by reducing ethyl phenylacetate with sodium and alcohol, and *phenylacetaldehyde*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CHO}$ (b.p. 206°), obtained by oxidising the alcohol, are used in perfumery; the former smells like roses, the latter like hyacinths. The aldehyde polymerises readily, giving various products.

β -Phenylpropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$ (hydrocinnamic acid), is conveniently prepared by reducing *cinnamic acid* (see below) with sodium amalgam and water,

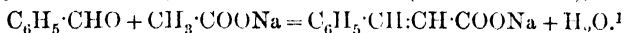


but may also be obtained from the product of the action of benzyl

chloride on ethyl sodiomalonate as already described (p. 462). It crystallises from water in needles, melts at 47° , and boils at 280° .

Cinnamic acid, $C_6H_5 \cdot CH:CH \cdot COOH$ (β -phenylacrylic acid), is closely related to β -phenylpropionic acid, and is perhaps the best-known *unsaturated* acid of the aromatic series. It occurs in large proportions in storax (*Styrax officinalis*), partly in the free state, and may be obtained by gently warming this vegetable product with caustic soda; the filtered aqueous solution of *sodium cinnamate* is treated with hydrochloric acid, and the precipitated cinnamic acid is purified by recrystallisation from light petroleum.

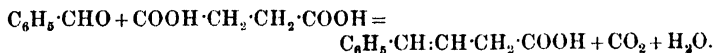
Cinnamic acid is prepared by heating benzaldehyde with acetic anhydride and anhydrous sodium acetate (*Perkin reaction*),



A mixture of benzaldehyde (10 parts), acetic anhydride (15 parts), and anhydrous sodium acetate (5 parts) is boiled in a flask heated in an oil-bath (air condenser). After about eight hours' time, the mixture is poured into water, and distilled in steam to separate any unchanged benzaldehyde; caustic soda is then added in excess, and the hot solution, filtered from oily and resinous impurities, is strongly acidified with hydrochloric acid; the precipitated cinnamic acid is purified by recrystallisation from boiling water.

This reaction is a very important one for the preparation of unsaturated aromatic acids, as, by employing the anhydrides and sodium salts of other aliphatic acids, homologues of cinnamic acid are obtained. When, for example, benzaldehyde is heated with sodium propionate and propionic anhydride, *phenylmethylacrylic acid* (α -methylcinnamic acid), $C_6H_5 \cdot CH:C(CH_3) \cdot COOH$, is formed; β -benzylidenepropionic acid, $C_6H_5 \cdot CH:CH \cdot CH_2 \cdot COOH$, is not obtained in this reaction, because combination always takes place between the aldehyde oxygen atom and the hydrogen atoms of that $-CH_2-$ group which is united with the carboxyl radical.

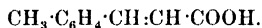
β -Benzylidenepropionic acid, however, may be prepared by heating benzaldehyde with a mixture of sodium succinate and succinic anhydride, carbon dioxide being eliminated,



It melts at 86° , and boils at 302° ; at its boiling-point, it is gradually converted into α -naphthol and water (p. 478).

¹ Possibly the aldehyde condenses with the anhydride and the product, $C_6H_5 \cdot CH:CH \cdot CO \cdot O \cdot CO \cdot CH_3$, is subsequently hydrolysed.

Other aldehydes which contain the aldehyde group directly united to the nucleus may be used in the Perkin reaction; the three *toluic aldehydes*, $\text{CH}_3\cdot\text{C}_6\text{H}_4\cdot\text{CHO}$, for example, give with sodium acetate and acetic anhydride the three (o.m.p.) *methylcinnamic acids*,



Cinnamic acid crystallises from water in needles, and melts at 133° . Its chemical behaviour, in many respects, is similar to that of acrylic acid and other unsaturated aliphatic acids; it combines directly with bromine, for example, yielding *β -phenyl- $\alpha\beta$ -dibromopropionic acid*, $\text{C}_6\text{H}_5\cdot\text{CHBr}\cdot\text{CHBr}\cdot\text{COOH}$, and with hydrogen bromide, giving *β -phenyl- β -bromopropionic acid*, $\text{C}_6\text{H}_5\cdot\text{CHBr}\cdot\text{CH}_2\cdot\text{COOH}$.

A solution of cinnamic acid in sodium carbonate immediately reduces a dilute solution of potassium permanganate at ordinary temperatures; all *unsaturated* acids show this behaviour, and are thus easily distinguished from saturated acids (Baeyer), but not from phenolic acids, phenols, and several other types of compounds which may reduce alkaline permanganate very readily. On reduction with sodium amalgam and water, cinnamic acid is converted into *β -phenylpropionic acid* (p. 462), just as acrylic acid is transformed into propionic acid.

When distilled with soda-lime, cinnamic acid is decomposed into carbon dioxide, and *phenylethylene* or *styrene*,¹



Concentrated nitric acid converts cinnamic acid into a mixture of about equal quantities of *o*- and *p*-*nitrocinnamic acids*,

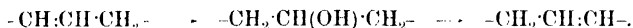


For their separation, these acids are converted into their ethyl esters, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{CH}\cdot\text{CH}\cdot\text{COOC}_2\text{H}_5$ (by means of alcohol and hydrogen chloride); the sparingly soluble ester of the *p*-acid separates, while the readily soluble *ethyl o-nitrocinnamate* remains in the solution. From the pure esters the acids are then regenerated, by hydrolysis with dilute sulphuric acid. They resemble cinnamic acid closely in properties, and combine directly with bromine, yielding the corresponding *nitrophenyl-dibromopropionic acids*, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{CHBr}\cdot\text{CHBr}\cdot\text{COOH}$.

¹ *Styrene*, $\text{C}_6\text{H}_5\cdot\text{CH}\cdot\text{CH}_2$, may be taken as a typical example of an aromatic hydrocarbon containing an *unsaturated* side-chain. It boils at 145° , and in chemical properties shows a very close resemblance to ethylene, of which it is the phenyl-substitution product. With bromine, for example, it yields a dibromo-additive product, $\text{C}_6\text{H}_5\cdot\text{CHBr}\cdot\text{CH}_2\text{Br}$ (*dibromoethylbenzene*), and when heated with hydriodic acid, it is reduced to *ethylbenzene*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_3$.

Stereoisomerism of Aromatic Olefinic Acids.—Some of the unsaturated acids of the aromatic series are known in stereoisomeric (*cis*- and *trans*-) forms, corresponding respectively with maleic and fumaric acids. *Allocinnamic acid*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{COOH}$, for example, is a stereoisomeride of cinnamic acid, and occurs, together with the latter, in certain by-products from the preparation of cocaine; it exists in three different crystalline modifications, melting at 42° , 58° , and 68° respectively, and probably represents the *cis* isomeride, in which the C_6H_5 - and $-\text{COOH}$ groups occupy positions corresponding with those of the two $-\text{COOH}$ groups in maleic acid (p. 280). *Cinnamylidenecetic acid* (see below) also exists in stereoisomeric forms, both of which are produced in the given reaction.

Many olefinic acids, not only of the aromatic, but also of the aliphatic series, undergo an interesting change when they are heated with concentrated aqueous alkalis. β -Benzylidenepropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CH}_2\cdot\text{COOH}$ (p. 463), for example, is partly converted into a *structural* isomeride, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}:\text{CH}\cdot\text{COOH}$, owing to the migration or shifting of the double binding from the $\beta\gamma$ - to the $\alpha\beta$ position. In such changes, particularly in the case of aliphatic acids, the general rule is, that the double binding in the molecule of the product is nearer to the carboxyl-group than that in the molecule of the original substance. The changes probably involve the addition and then the elimination of the elements of water, and are usually reversible :

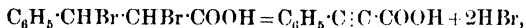


Cinnamic aldehyde, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CHO}$, is the principal component of oil of cinnamon, from which it may be extracted with the aid of a solution of sodium hydrogen sulphite. It may be obtained by heating a mixture of the calcium salts of cinnamic and formic acids, or by condensing benzaldehyde with acetaldehyde, in the presence of sodium ethoxide.

It boils at 252° , and has a characteristic aromatic odour; on exposure to the air, it is oxidised to cinnamic acid. Its *hydrazone* melts at 168° . Cinnamic aldehyde, like benzaldehyde, condenses readily with many other compounds; thus, when treated with malonic acid, in the presence of pyridine, it gives *cinnamylidenemalonic acid*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CH}:\text{C}(\text{COOH})_2$, which decomposes into *cinnamylidenecetic acid*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CH}:\text{CH}\cdot\text{COOH}$, and carbon dioxide when it is heated (p. 246).

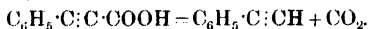
Many other unsaturated acids, both aliphatic and aromatic, are prepared by condensing an aldehyde with malonic acid.

Phenylpropionic acid, $\text{C}_6\text{H}_5\cdot\text{C}:\text{C}\cdot\text{COOH}$, is obtained by treating phenyl- $\alpha\beta$ -dibromopropionic acid (p. 464), or its ethyl ester, with alcoholic potash,

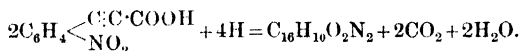


a method which is exactly similar to that employed in preparing acetylene by the action of alcoholic potash on ethylene dibromide. It melts at 137° , and at higher temperatures, or when heated with

water at 120°, it decomposes into carbon dioxide and *phenylacetylene*, a colourless liquid (b.p. 140°) which is closely related to *acetylene* in chemical properties,



o-Nitrophenylpropionic acid, $\text{C}_6\text{H}_4(\text{NO}_2)\cdot\text{C}\equiv\text{C}\cdot\text{COOH}$, may be similarly prepared from *o*-nitrophenyldibromopropionic acid; when treated with reducing agents, such as hydrogen sulphide, or glucose and alkali, it is converted into indigo-blue (Baeyer),



This method of preparation, however, is not of technical value.

CHAPTER XXXII.

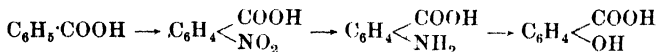
PHENOLIC AND HYDROXY-CARBOXYLIC ACIDS.

THE hydroxy-acids of the aromatic series are derived from benzoic acid and its homologues, by the substitution of hydroxyl-groups for hydrogen atoms; like the simple hydroxy-derivatives of the aromatic hydrocarbons, they may be divided into two classes, according as the hydroxyl-group is united with carbon of the nucleus or of the side-chain. In the first case, the hydroxyl-group has the same character as in phenols, and consequently hydroxy-acids of this class, as, for example, the three (*o.m.p.*) *hydroxybenzoic acids*, $\text{C}_6\text{H}_4(\text{OH})\cdot\text{COOH}$, are both phenols and carboxylic acids; in the second case, however, the hydroxyl-group has the same character as in alcohols, so that the compounds of this class, such as *mandelic acid*, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{COOH}$, have properties resembling those of aliphatic hydroxy-acids; in other words, the differences between the two classes of aromatic hydroxy-acids are practically the same as those between phenols and alcohols.

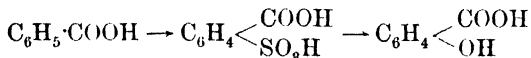
As those acids which contain the hydroxyl-group united with carbon of the nucleus form by far the more important class, they will be described first, and the following statements refer to them only.

Preparation.—The phenolic acids may be prepared from the simple carboxylic acids, by reactions exactly similar to those employed in the preparation of phenols from hydrocarbons; that

is to say, the acids are converted into nitro-compounds, then into amino-compounds, and the latter are treated with nitrous acid in the usual manner,



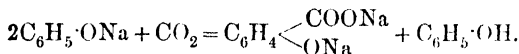
or, the acids are heated with sulphuric acid, and the sulphonic acids obtained in this way are fused with a caustic alkali,



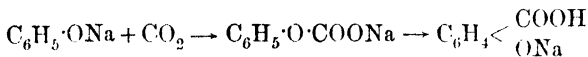
It must be borne in mind, however, that as the carboxyl-group of the acid determines the position taken up by the nitro- and sulphonic-groups (p. 382), only the *m*-hydroxy-compounds are formed by these two methods.

The *o*-phenolic acids, and in some cases the *p*-compounds, are most conveniently prepared from the phenols by one of the following methods:

The *dry* sodium compound of a phenol is heated at about 200° in a stream of carbon dioxide (Kolbe),



Under these conditions half the phenol distils over and is recovered; but if the sodium phenate is saturated with carbon dioxide under pressure at about 100°, it is converted into *sodium phenylcarbonate*, which, at about 130° under pressure, is transformed into a derivative of the phenolic acid,

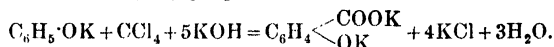


The sodium phenylcarbonate decomposes into carbon dioxide and sodium phenate, which re-unite to form the final product.

Many dihydric and trihydric phenols may be converted into phenolic acids, by merely heating them in aqueous solution with ammonium (or potassium) hydrogen carbonate; when resorcinol, for example, is treated in this way, it yields a mixture of isomeric *resorcylic acids*, $\text{C}_6\text{H}_3(\text{OH})_2\cdot\text{COOH}$. This reaction affords a striking illustration of the readiness with which hydrogen atoms of the nucleus may be displaced in the case of certain substitution products of benzene (compare pp. 393, 425).

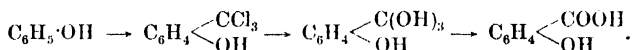
The second general method for the preparation of phenolic

acids from phenols consists in boiling a strongly alkaline solution of the phenol with carbon tetrachloride; the principal product is the **p**-acid, but varying proportions of the **o**-acid are also formed,

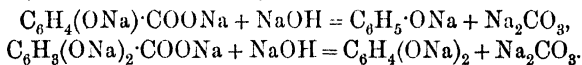


The phenol (1 mol.) is dissolved in a concentrated aqueous solution of potassium hydroxide (6 mols.), carbon tetrachloride (1 mol.), and enough alcohol to form a homogeneous solution are added, and finally a small proportion of precipitated copper. After the substances have been heated together during 8-10 hours, any unchanged carbon tetrachloride is steam-distilled, water is added, and the filtered aqueous solution is treated with an excess of acid and extracted with ether; the ethereal extract is then shaken with a solution of sodium carbonate, which extracts the acids, leaving any phenol dissolved in the ether. The phenolic acids are then precipitated with a mineral acid, and purified by recrystallisation.

This method is an extension of that of Tiemann and Reimer (p. 442), and it may be assumed that the changes which occur take place in various stages, as indicated below:



Properties. --The phenolic acids are colourless, crystalline substances, more readily soluble in water, and less volatile, than the acids from which they are derived; many of them undergo decomposition when heated strongly, carbon dioxide being evolved; when heated with soda-lime they are all decomposed, with formation of (sodium derivatives of) phenols,



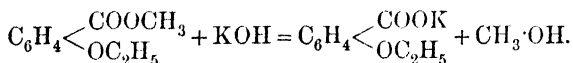
The **o**-acids, as, for example, *salicylic acid*, give, in neutral aqueous solution, a violet colouration with ferric chloride, whereas the **m**- and **p**-acids, such as the **m**- and **p**-hydroxybenzoic acids, give no colouration.

The phenolic acids show the chemical properties of both phenols and carboxylic acids. As carboxylic acids, they form salts by the displacement of the hydrogen atom of the carboxyl-group, such salts being obtained when the acids are treated with carbonates or with one equivalent of a metallic hydroxide; when, however, excess of alkali hydroxide is employed, the hydrogen atom of the phenolic group is also displaced, just as in the case of phenols. Phenolic acids, therefore, form both mono- and di-metallic

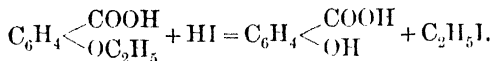
salts; *salicylic acid*, for example, yields the two sodium salts, $C_6H_4(OH) \cdot COONa$ and $C_6H_4(ONa) \cdot COONa$.

The di-metallic salts are decomposed by carbonic acid, giving mono-metallic salts, just as the phenates give phenols; the metal in combination with the carboxyl-group, however, cannot be displaced in this way.

The *esters* of the phenolic acids are prepared in the usual manner—namely, by saturating a solution of the acid in excess of the alcohol with hydrogen chloride (p. 172); by this treatment the hydrogen of the carboxyl-group only is displaced, ordinary esters, such as *methyl salicylate*, $C_6H_4(OH) \cdot COOCH_3$, being formed. These compounds still have phenolic properties, and dissolve in caustic alkalis, forming metallic derivatives, such as *potassium methyl salicylate*, $C_6H_4(OK) \cdot COOCH_3$, which, with alkyl halides or dimethyl sulphate, yield alkyl-derivatives, such as *methyl o-ethoxybenzoate*,¹ $C_6H_4(OC_2H_5) \cdot COOCH_3$. On hydrolysis with alcoholic potash, only the alkyl of the carboxyl-group is displaced from di-alkyl compounds of this kind; methyl ethoxybenzoate, for example, yields the potassium salt of ethoxybenzoic acid,



The other alkyl-group is not eliminated even by boiling alkalis, a behaviour which corresponds with that of the alkyl-group in derivatives of phenols, such as *anisole*, $C_6H_5 \cdot OCH_3$ (p. 426). Just, however, as anisole is decomposed into phenol and methyl iodide when it is heated with hydriodic acid, so ethoxybenzoic acid, under similar conditions, yields the phenolic acid (compare p. 528),



Salicylic acid, $C_6H_4(OH) \cdot COOH$ (*o* hydroxybenzoic acid), occurs in the blossom of *Spiræa ulmaria*, and is also found in considerable quantities, as *methyl salicylate*, in oil of wintergreen (*Gaultheria procumbens*). It used to be prepared, especially for pharmaceutical purposes, by hydrolysing this oil with potash.

Salicylic acid may be obtained by oxidising *salicylaldehyde*

¹ This compound might be called *methyl ethylsalicylate*, but such a name would be ambiguous, as it might also be given to the various isomerides of the formula, $C_6H_3(C_2H_5)(OH) \cdot COOCH_3$.

(p. 442), or *salicyl alcohol* (saligenin, p. 471), with chromic acid, by treating *o*-aminobenzoic acid (anthranilic acid, p. 455) with nitrous acid, and also by boiling *phenol* with caustic soda and carbon tetrachloride (p. 468).

It is prepared on the large scale by treating *dry* sodium phenate with carbon dioxide under pressure, first at about 100° and then at about 120 – 140° (compare p. 467); the product is dissolved in water, and the salicylic acid is precipitated with hydrochloric acid.

Salicylic acid is sparingly soluble in cold (1 in 400 parts at 15°), but readily so in hot, water, from which it crystallises in needles, melting at 155° ; its neutral solutions give with ferric chloride an intense violet colouration. When rapidly heated it sublimes, and only slight decomposition occurs; but when distilled slowly, it decomposes to a great extent into phenol and carbon dioxide, this change being complete if the acid is heated with soda-lime.

When salicylic acid is reduced with sodium and boiling amyl alcohol, it is converted into normal *pimelic acid*, $\text{COOH} \cdot [\text{CH}_2]_5 \cdot \text{COOH}$ (p. 261)¹; in a similar manner, certain other *o*-phenolic acids (but not the *m*- or *p*- compounds) may be transformed into homologues of pimelic acid.

Salicylic acid is a powerful antiseptic, and, as it has no smell, it is frequently used as a disinfectant instead of phenol; it is also employed in medicine and in the manufacture of azo-dyes.

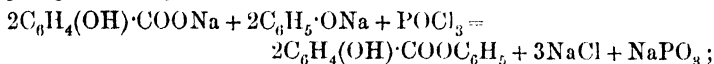
The mono-metallic salts of salicylic acid, such as, for example, *potassium salicylate*, $\text{C}_6\text{H}_4(\text{OH}) \cdot \text{COOK}$, and *calcium salicylate*, $\{\text{C}_6\text{H}_4(\text{OH}) \cdot \text{COO}\}_2\text{Ca}$, are prepared by neutralising a hot aqueous solution of the acid with metallic carbonates; most of them are soluble in water. The di-metallic salts, such as $\text{C}_6\text{H}_4(\text{OK}) \cdot \text{COOK}$ and $\text{C}_6\text{H}_4 \cdot \begin{smallmatrix} \text{O} \\ \diagup \quad \diagdown \\ \text{COO} \end{smallmatrix} \text{Ba}$, are obtained in a similar manner, employing excess of the metallic hydroxides; with the exception of those of the alkali metals, they are almost insoluble in water and are decomposed by carbonic acid, giving the mono-metallic salts.

Methyl salicylate, $\text{C}_6\text{H}_4(\text{OH}) \cdot \text{COOCH}_3$, may be prepared in the manner described (p. 469), or by distilling a mixture of salicylic acid, methyl alcohol, and sulphuric acid (p. 172); it is a very pleasant-smelling oil, boiling at 224° ; **ethyl salicylate**,

¹ By the addition of 4H, the acid is probably converted into an enol containing the group, $-\text{C}(\text{OH}) \cdot \text{C}(\text{COOH})-$, which, after isomeric change into a β -ketonic acid, undergoes acid hydrolysis (p. 184).

$C_6H_4(OH) \cdot COOC_2H_5$, boils at 231.5° . These and other esters are immediately converted into solid sodium derivatives by concentrated solutions of alkalis, but when water is then added and the solutions are boiled, the esters undergo hydrolysis.

Phenyl salicylate, $C_6H_4(OH) \cdot COOC_6H_5$, is prepared by heating a mixture of sodium salicylate and sodium phenoxide with phosphorus oxychloride,



it melts at $42-43^\circ$, is almost odourless, and is much employed in medicine and in surgery, under the name of *salol*, in the place of salicylic acid. It is practically insoluble in water and its alcoholic solution gives a violet colouration with ferric chloride.

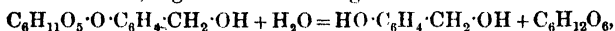
Acetylsalicylic acid, $C_6H_4(OAc) \cdot COOH$ (*aspirin*), obtained by heating salicylic acid with acetic anhydride or acetyl chloride, is also an important drug; it melts at 135° and is very sparingly soluble in water. Its aqueous solution gives no colouration with ferric chloride, but does so after having been boiled during some time.

Methyl o-methoxybenzoate, $C_6H_4(OCH_3) \cdot COOCH_3$, is formed when methyl salicylate is heated with methyl iodide and potash (1 mol.) in alcoholic solution; it is an oil, boiling at 245° , and gives a salt of o-methoxybenzoic acid, $C_6H_4(OCH_3) \cdot COOH$ (m.p. 98.5°), when it is hydrolysed with aqueous alkali.

m-Hydroxybenzoic acid is prepared by fusing **m-sulphobenzoic acid** with alkali, and also by the action of nitrous acid on **m-aminobenzoic acid**. It melts at 200° .

p-Hydroxybenzoic acid is formed, together with salicylic acid, by the action of carbon tetrachloride and potash on phenol; it may also be obtained from **p-sulphobenzoic acid** by fusion with alkali, or by the action of nitrous acid on **p-aminobenzoic acid**. It is prepared by heating dry potassium phenate in a stream of carbon dioxide at 220° so long as phenol distils over; if, however, the temperature be kept below 150° , potassium salicylate is formed. **p-Hydroxybenzoic acid** melts at 210° .

Saligenin, $C_6H_4(OH) \cdot CH_2 \cdot OH$ (**o-hydroxybenzyl alcohol**, *salicyl alcohol*), is an example of a substance which is both a phenol and an alcohol. It is produced, together with glucose, by the action of dilute acids or enzymes on *salicin*, a glucoside occurring in the bark of the willow-tree,



and may be prepared by reducing salicylaldehyde (p. 442) with sodium amalgam and aqueous alcohol.

Saligenin melts at 86° , and is readily soluble in water; the solution

becomes deep blue on the addition of ferric chloride. Owing to its phenolic nature, it forms alkali salts, which, when heated with alkyl halides, give the corresponding ethers; on the other hand, it shows the properties of an alcohol, and yields salicylaldehyde and salicylic acid on oxidation.

Salicin, $C_6H_{11}O_5 \cdot O \cdot C_6H_4 \cdot CH_2 \cdot OH$, melts at 201° and chars when strongly heated; it is readily soluble in hot water, and when hydrolysed by boiling dilute acids it gives saligenin (p. 471), and also glucose, which can be tested for with Fehling's solution. It is turned red by concentrated sulphuric acid.

The *m*- and *p*-hydroxybenzyl alcohols may be prepared by the reduction of the *m*- and *p*-hydroxybenzaldehydes (p. 443); they melt at 67° and 110° respectively.

Anisyl alcohol, $C_6H_4(OCH_3) \cdot CH_2 \cdot OH$ (*p* methoxybenzyl alcohol), is obtained by treating *anisaldehyde*, $C_6H_4(OCH_3) \cdot CHO$ (p. 443), with sodium amalgam and aqueous alcohol, or with alcoholic potash (Cannizzaro reaction); also by heating *p*-hydroxybenzyl alcohol with caustic alkali and methyl iodide in alcoholic solution. It melts at 25° , and boils at 258° ; on oxidation, it yields *anisaldehyde* and *anisic acid*.

Anisic acid, $C_6H_4(OCH_3) \cdot COOH$ (*p* methoxybenzoic acid), is obtained by oxidising *anethole*, $C_6H_4(OCH_3) \cdot CH:CH \cdot CH_3$ (the principal component of oil of aniseed), with chromic acid; it may also be prepared by methylating *p*-hydroxybenzoic acid.

It melts at 185° , and when heated with soda-lime it is decomposed, with the formation of *anisole* (p. 426); when heated with fuming hydriodic acid, it yields *p*-hydroxybenzoic acid and methyl iodide.

There are six *dihydroxybenzoic acids*, $C_6H_3(OH)_2 \cdot COOH$, two of which are derived from catechol, three from resorcinol, and one from quinol; the most important of these is **protocatechuic acid** [$COOH:OH:OH = 1:3:4$], one of the two isomeric *catecholcarboxylic acids*. This compound is formed when many resins, such as catechu and gum benzoin, and also certain alkaloids, are fused with potash; it may be prepared synthetically by heating catechol with water and ammonium hydrogen carbonate at 140° (p. 467).

It melts at 199° , is very soluble in water, and when strongly heated, it is decomposed into catechol and carbon dioxide; its aqueous solution gives with ferric chloride a green solution, which becomes violet and then red on the addition of sodium hydrogen carbonate.

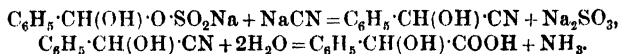
Gallic acid, $C_6H_2(OH)_3 \cdot COOH$ [$3OH = 3:4:5$] (or pyrogallol-carboxylic acid), is a trihydroxybenzoic acid; it occurs in gall-nuts, tea, and many other vegetable products, and is best prepared by boiling *tannin* (see below) with dilute acids. It crystall-

ises in needles, and melts at 220° , being at the same time resolved into pyrogallol (p. 433) and carbon dioxide; it is readily soluble in water, and its aqueous solution gives with ferric chloride a bluish-black precipitate. Gallic acid is a strong reducing agent, and precipitates gold, silver, and platinum from solutions of their salts.

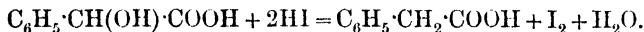
Tannin (tannic acid) is the name given to a vegetable product which occurs in large quantities in gall-nuts, sumach, and in many kinds of bark, from which it may be extracted with boiling water. It is an almost colourless, amorphous substance, and is readily soluble in water; its solutions have a very astringent taste, and give with ferric chloride an intense dark-blue solution, for which reason tannin is employed in the manufacture of inks. Tannin is used in dyeing, as a mordant, owing to its property of forming insoluble coloured compounds with many dyes (p. 582). It is also extensively employed in tanning. When animal skin or membrane, after suitable preliminary operations, is placed in a solution of tannin, or in contact with moist bark containing tannin, it absorbs and combines with the tannin, and is converted into a much tougher material; such tanned skins constitute leather.

When boiled with dilute sulphuric acid, *some* tannins are completely converted into gallic acid and glucose, a fact which seems to show that these substances are probably glucosides, derived from glucose by the displacement of hydroxylic hydrogen atoms by *galloyl*, $\text{C}_6\text{H}_2(\text{OH})_3\cdot\text{CO}-$ (or *digalloyl*-) groups. As, however, tannins are amorphous and ill-characterised substances, little is known as to their structure, and many of them may be mixtures of variable composition.

Mandelic acid, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{COOH}$ (phenylglycollic acid), is an example of an aromatic hydroxy-acid containing the hydroxyl-group in the *side-chain*. It may be obtained by boiling amygdalin (benzaldehyde cyanohydrin, combined with glucose, p. 310) with concentrated hydrochloric acid; it is usually prepared by treating the solid bisulphite compound of benzaldehyde with a concentrated solution of sodium cyanide and hydrolysing the oily hydroxycyanide (*mandelonitrile*), which is thus produced, with boiling concentrated hydrochloric acid,



Mandelic acid is moderately soluble in water, and shows the general behaviour of a hydroxy-acid; when heated with hydriodic acid, for example, it is reduced to *phenylacetic acid* (p. 462), just as lactic acid is reduced to propionic acid (p. 252),



The hydroxyl-group in mandelic acid has an aliphatic character similar to that of the hydroxyl-group in glycollic acid, and in the alcohols, so that there are many points of difference between mandelic acid and phenolic acids, such as salicylic acid, which contain the hydroxyl-group united with carbon of the nucleus. When, for example, *ethyl mandelate*, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{COOC}_2\text{H}_5$, is treated with caustic alkalis it does *not* yield an alkali derivative, but the hydrogen of the hydroxyl-group is displaced when the ester is treated with sodium or potassium.

Mandelic acid, like lactic acid, exists in optically different forms. The synthetical acid (m.p. 118°) is a *dL*-substance, but the acid (m.p. 133°) prepared from amygdalin is lævorotatory.

CHAPTER XXXIII.

NAPHTHALENE AND ITS DERIVATIVES.

ALL the aromatic hydrocarbons hitherto described, with the exception of diphenyl, diphenylmethane, and triphenylmethane (p. 370), contain only *one* closed-chain of six carbon atoms, and are very closely and directly related to benzene; most of them may be prepared from benzene, and reconverted into this hydrocarbon, by comparatively simple reactions, so that they may all be classed as direct benzene derivatives. The exceptions just mentioned are also closely related to benzene, although they might be regarded as hydrocarbons of quite another class, because diphenyl and diphenylmethane contain two, and triphenylmethane contains three, closed-chains of six carbon atoms. There are, however, other classes, or types, of aromatic hydrocarbons more distantly related to benzene, and of these *naphthalene*, which is now to be described, is perhaps second only to benzene in importance; it is the parent substance of a great number of

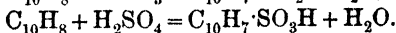
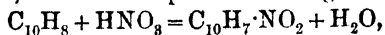
compounds, many of which are extensively employed in the manufacture of dyes.

Naphthalene, $C_{10}H_8$, occurs in coal-tar in larger quantities than does any other hydrocarbon, and is easily isolated from this source in a pure condition. The crystals of crude naphthalene, which are deposited from the fraction of coal-tar passing over between 170° and 230° (*middle oil*, p. 327), are first pressed to get rid of liquid impurities, then washed with caustic soda, and finally warmed with a small quantity of concentrated sulphuric acid, which converts most of the foreign substances into soluble sulphonic acids; the naphthalene is then distilled or sublimed.

Naphthalene crystallises in large, lustrous plates, melts at 80° , and boils at 218° . It has a highly characteristic smell, and is extraordinarily volatile, considering its high molecular weight—so much so, in fact, that only part of the naphthalene in crude coal-gas is deposited in the condensers (p. 325); the rest is carried forward into the purifiers, and even into the gas-mains, where, in very cold weather, it may be deposited in crystals and cause stoppages at the bends of the pipes. It is insoluble in water, but dissolves freely in many organic solvents, from which it may be crystallised. Like some other aromatic hydrocarbons, it crystallises with picric acid, and when concentrated benzene solutions of the two substances are mixed, *naphthalene picrate*, $C_{10}H_8 \cdot C_6H_2(NO_2)_3 \cdot OH$, is precipitated in yellow needles, which melt at 149° .

Naphthalene is employed as a disinfectant or insecticide and for the preparation of phthalic acid (p. 457), but its principal use is for the manufacture of a great many derivatives, which are employed in the colour industry.

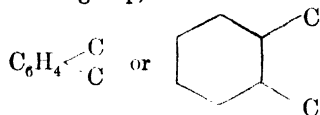
Constitution.—Naphthalene has the characteristic properties of an aromatic compound, which means that its behaviour under various conditions is similar to that of benzene and its derivatives, and different from that of aliphatic compounds. It is attacked by halogens, nitric acid, and sulphuric acid, giving substitution products: with nitric acid, for example, it yields *nitro-derivatives*, and with sulphuric acid it gives *sulphonic acids*,



This similarity between benzene and naphthalene at once suggests

a resemblance in constitution, a view which is confirmed by the fact that naphthalene, like benzene, is a very stable compound, and is resolved into simpler substances only with difficulty. When, however, naphthalene is boiled with chromic acid or dilute nitric acid, or with concentrated sulphuric acid (p. 457), it is slowly oxidised, yielding carbon dioxide, water, and (*ortho*-) phthalic acid, $C_6H_4(COOH)_2$.

Now the formation of phthalic acid in this way is a fact of very great importance, since it is a proof that the molecule of naphthalene contains the group,

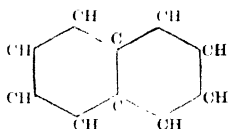


—that is to say, that it contains a benzene nucleus to which two carbon atoms are united in the *ortho*-position to one another. This fact alone, however, is insufficient to establish the constitution of the hydrocarbon, since there are still two atoms of carbon and four of hydrogen to be accounted for, and there are various ways in which these might be united with the $\begin{array}{c} \text{C} \\ \diagup \quad \diagdown \\ \text{C} \end{array}$ group.

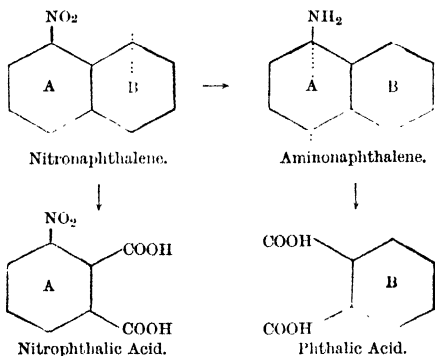
Clearly, therefore, it is important to ascertain the structure of that part of the naphthalene molecule, which has been oxidised to carbon dioxide and water—to obtain, if possible, some decomposition product of known constitution, in which these carbon and hydrogen atoms are retained in their original state of combination.

Now this can be done in the following way: When *nitronaphthalene*, $C_{10}H_7NO_2$, a simple mono-substitution product of the hydrocarbon, is boiled with dilute nitric acid, it yields *nitrophthalic acid*, $C_6H_3(NO_2)(COOH)_2$; naphthalene, therefore, contains a benzene nucleus, and the nitro-group in nitronaphthalene is combined with this nucleus. If, however, the *same* nitronaphthalene is reduced to *aminonaphthalene*, $C_{10}H_7NH_2$, and the latter is oxidised, *phthalic acid* (and not aminophthalic acid) is obtained. This last fact can only be explained on the assumption either that the benzene nucleus, which is known to be united with the amino-group, has been destroyed, or that the amino-group has been displaced by *hydrogen* during oxidation. Since, however,

the latter alternative is contrary to experience, the former must be accepted, and it must be concluded that the benzene nucleus which is contained in the oxidation product of aminonaphthalene is *not the same* as that present in the oxidation product of nitronaphthalene; in other words, different parts of the naphthalene molecule have been oxidised to carbon dioxide and water in the two cases, and yet in both these reactions the group, $C_6H_4 \begin{smallmatrix} \diagup C \\ \diagdown C \end{smallmatrix}$ remains. The constitution of naphthalene, therefore, may be provisionally and partly expressed by the formula or symbol,



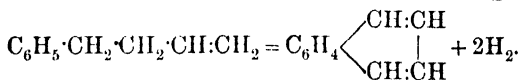
This conclusion will be obvious if the above changes are now represented with the aid of this formula, the symbols C and H being omitted for the sake of simplicity. When nitronaphthalene is oxidised, the nucleus B (see below), which does not contain the nitro-group, is disintegrated (as indicated by the dotted lines), the product being nitrophthalic acid; when, on the other hand, aminonaphthalene is oxidised, the nucleus A, combined with the amino-group, is attacked, and, together with the amino-group undergoes disintegration, phthalic acid being formed:



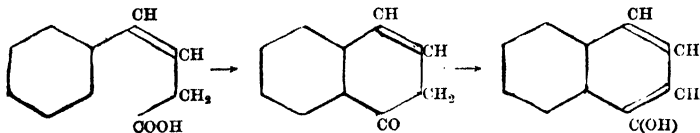
It was in this way that Graebe determined the constitution of naphthalene in 1880; he proved that (as had been suggested by

Erlenmeyer as early as 1866) its molecule contains two benzene nuclei *condensed* together in the *o*-position, that is to say, having two *o*-carbon atoms in common, as shown above. Further evidence supporting this conclusion has since been obtained from syntheses of naphthalene and its derivatives, and from the results of the study of the isomerism of its substitution products.

Naphthalene may be obtained synthetically by passing the vapour of *phenylbutylene*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}:\text{CH}_2$ ¹ (or of *phenylbutylene dibromide*, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHBr}\cdot\text{CH}_2\text{Br}$), over red-hot lime; the change involves the loss of hydrogen, as in the formation of other aromatic, from aliphatic, hydrocarbons (p. 330),



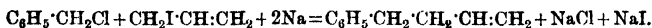
A most important synthesis of naphthalene was accomplished by Fittig, who showed that *α-naphthol* (*α*-hydroxynaphthalene) is formed when *β*-benzylidenepropionic acid (a substance of *known* constitution, p. 463) is heated at about 300°. This reaction may take place in two stages, the first product being a keto-derivative of naphthalene, which passes into *α*-naphthol by intramolecular or tautomeric change (compare p. 189).



The *α*-naphthol thus obtained may be converted into naphthalene by distillation with zinc-dust, just as phenol may be transformed into benzene (p. 362).

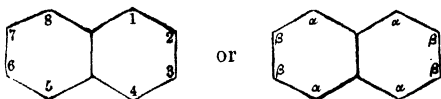
Isomerism of Naphthalene Derivatives.—As in the case of benzene, the study of the isomerism of its substitution products affords the most convincing evidence as to the fundamental structure of naphthalene. In the first place, this hydrocarbon differs from benzene in yielding *two* isomeric *mono*-substitution products; there are, for

¹ *Phenylbutylene* is obtained by treating a mixture of benzyl chloride and allyl iodide with sodium,



It is a liquid, boiling at 178°, and, like butylene, it combines directly with one molecule of bromine, yielding the dibromide.

example, two *monochloronaphthalenes*, two *monohydronaphthalenes*, two *mononitronaphthalenes*, &c. This fact is readily accounted for with the aid of the formula or symbol given on p. 477, which may be conveniently written,



(numbered or lettered as above, the symbols C and H being omitted for the sake of simplicity), and which shows that the eight hydrogen atoms are not all similarly situated relatively to the rest of the molecule. If, for example, the hydrogen atom at (1) were displaced by chlorine, hydroxyl, &c., the substitution product would not be identical with the corresponding compound produced by the displacement of the hydrogen atom (2). In the first case the substituent would be united with a carbon atom, which is itself directly combined with one of the carbon atoms common to both nuclei, whereas, in the other case, this would not be so. Further, it will be seen that no more than *two* such isomerides could be obtained, because the positions 1, 4, 5, 8 (the four α -positions) are identical, and so also are the positions 2, 3, 6, 7 (the four β -positions). Clearly, then, the fact that the *mono*-substitution products of naphthalene exist in *two* isomeric forms is in accordance with the given constitutional formula; these isomeric *mono*-substitution products are usually distinguished with the aid of the letters α and β .

When *two* hydrogen atoms in naphthalene are displaced by two identical groups or atoms, *ten* isomeric di-derivatives may be obtained. The positions of the substituents being indicated by the numerals already used, these isomerides would be,

1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 2:3, 2:6, 2:7,

and all other possible positions would be identical with one of these; 2:5, for example, is the same as 1:6, 4:7, and 3:8, and 1:5 is identical with 4:8. The constitution of such a *di*-derivative is usually expressed with the aid of numerals in this manner; 1:2-hydroxyaminonaphthalene, and 1:5-hydroxyaminonaphthalene, $C_{10}H_6(OH) \cdot NH_2$, for example, are thus distinguished, and the structure of each compound is shown.

When the two atoms or groups are present in one and the

same nucleus, their relative positions are similar to those of groups in the *o*-, *m*-, or *p*-position in benzene. The positions 1:2, 2:3, and 3:4 correspond with the *ortho*-, 1:3 and 2:4 with the *meta*-, and 1:4 with the *para*-position, and similarly in the case of the other nucleus. The position 1:8 or 4:5, however, is different from any of these, and is termed the *peri*-position; groups thus situated behave in much the same way as those in the *o*-position in the benzene and naphthalene nuclei (pp. 492, 503).

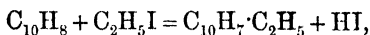
The difficulty of determining and of expressing the actual state or disposition of the fourth unit of valency of each of the carbon atoms in naphthalene is much the same as in the case of benzene. If the carbon atoms are represented as united by alternate double linkings, as in either of the formulæ given below, there is the objection that the carbon atoms do not show, as indicated, the behaviour of those in aliphatic unsaturated compounds.



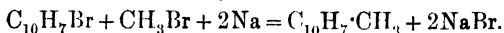
For reasons similar to those considered in the case of benzene (p. 336), the molecule of naphthalene is therefore represented by a simple double hexagon; this symbol summarises the main facts concerning its chemical behaviour and also accounts for the isomerism of its derivatives.

Derivatives of Naphthalene.

The *homologues of naphthalene*—that is to say, its *alkyl substitution products*—are of comparatively little importance; they may be prepared from the parent hydrocarbon by methods similar to those employed in the case of the corresponding benzene derivatives, as, for example, by treating naphthalene with alkyl halides in the presence of aluminium chloride (Friedel and Crafts' reaction),



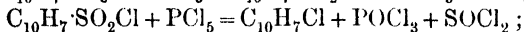
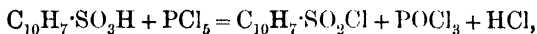
and by treating the bromonaphthalenes with an alkyl halide and sodium (Wurtz-Fittig reaction),



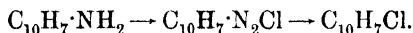
α-Methylnaphthalene, $\text{C}_{10}\text{H}_7\cdot\text{CH}_3$, is a colourless liquid, boiling at 240–242°, but *β-methylnaphthalene* is a solid, melting at 32°, and boiling at 242°; both these hydrocarbons occur in coal-tar.

The *halogen mono-substitution products* of naphthalene are also of little importance. They may be obtained by treating the

hydrocarbon, at its boiling-point, with the halogens (chlorine and bromine), but only the α -derivatives are formed in this way. Both the α - and the β -compounds may be obtained by treating the corresponding naphthols (p. 485), or, much better, the naphthalenesulphonic acids (p. 486), with pentachloride or pentabromide of phosphorus,



also by converting the naphthylamines (p. 483) into the corresponding diazonium-compounds, and decomposing the latter with a halogen cuprous salt (Sandmeyer reaction, p. 402) or with copper powder (p. 403),



All these methods correspond with those described in the case of the halogen derivatives of benzene, and are carried out in a similar manner practically.

α -Chloronaphthalene, $\text{C}_{10}\text{H}_7\text{Cl}$, is a liquid, boiling at about 263° , but the *β -derivative* is a crystalline substance, melting at 56° , and boiling at 265° .

α -Bromonaphthalene, $\text{C}_{10}\text{H}_7\text{Br}$, is also a liquid at ordinary temperatures, and boils at 279° , but the *β -derivative* is crystalline, and melts at 59° .

The chemical properties of these, and of other halogen derivatives of naphthalene, are similar to those of the halogen derivatives of benzene; the halogen atoms are very firmly combined, and cannot be displaced by hydroxyl-groups with the aid of aqueous alkalis, &c.

Naphthalene tetrachloride, $\text{C}_{10}\text{H}_8\text{Cl}_4$, is an important halogen additive product, which is produced when chlorine is passed into coarsely powdered naphthalene, at ordinary temperatures. It forms large colourless crystals, melts at 182° , and is converted into *dichloronaphthalenes*, $\text{C}_{10}\text{H}_6\text{Cl}_2$ (substitution products of naphthalene), when it is heated with alcoholic potash; it is readily oxidised by nitric acid, yielding phthalic and oxalic acids, a fact which shows that all the chlorine atoms are united with one and the same nucleus; the constitution of the compound, therefore, is expressed by the formula, $\text{C}_6\text{H}_4 \begin{matrix} \text{CHCl} \cdot \text{CHCl} \\ \text{CHCl} \cdot \text{CHCl} \end{matrix}$.

The formation of this additive product shows that naphthalene, like benzene, is not really a saturated compound, although it usually behaves as such. Many other additive compounds have been obtained; such substances may be produced by the reduction of certain substitution products of naphthalene with sodium and boiling amyl alcohol, but a much more important general method is by the reduction of naphthalene and its derivatives with hydrogen in the presence of nickel (Sabatier-Senderens, p. 357). In such reactions first *four*, and then *six* more hydrogen atoms are usually taken up, and in the first stage the addition is restricted to *one* only of the two benzene nuclei. When a naphthalene derivative is thus converted into a tetrahydro-additive compound, the atoms or groups directly united with the reduced nucleus acquire the properties which they have in aliphatic compounds, whereas those united to the unreduced nucleus retain the properties which they have in nuclear substitution products of benzene. The amino-group in

ac.-tetrahydro-β-naphthylamine, $C_6H_4 \begin{matrix} \text{CH}_2 \cdot \text{CH} \cdot \text{NH}_2 \\ | \\ \text{CH}_2 \cdot \text{CH}_2 \end{matrix}$, for example, has

the same character as that in aliphatic amines, whereas in the case of

the isomeric *ar.-tetrahydro-β-naphthylamine*, $\text{NH}_2 \cdot C_6H_3 \begin{matrix} \text{CH}_2 \cdot \text{CH}_2 \\ | \\ \text{CH}_2 \cdot \text{CH}_2 \end{matrix}$, the

amino-group has the same properties as that in aniline, because it is combined with the unreduced nucleus. Such tetrahydro-derivatives of naphthalene are distinguished by the prefixes *ar.-* (aromatic) or *ac.-* (alicyclic), according as the substituent is contained in the unreduced or in the reduced nucleus. *α*-Naphthylamine and *α*-naphthol are reduced to *ar.-tetrahydro*-compounds by sodium and boiling amyl alcohol, but *β*-naphthylamine and *β*-naphthol give the *ac.-tetrahydro*-compounds as principal products, and smaller quantities of the *ar.-tetrahydro*-derivatives. *ar.-Tetrahydronaphthol* is phenolic in character, but the *ac.-isomeride* has the properties of an aliphatic alcohol.

Tetrahydronaphthalene (*tetralene*), $C_{10}H_{12}$, and **decahydronaphthalene** (*decalane*), $C_{10}H_{18}$, are now prepared on the large scale by the reduction of naphthalene with hydrogen (and nickel); they are liquids, boiling at 207° and *about* 187° respectively, and are used as solvents.

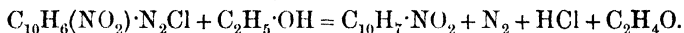
Nitro-Derivatives.—Naphthalene, like benzene, is readily *nitrated* by a mixture of nitric and sulphuric acids, giving mono- and di-nitro-derivatives. The chemical properties of the nitro-naphthalenes are in nearly all respects similar to those of the nitrobenzenes.

α-**Nitronaphthalene**, $C_{10}H_7 \cdot \text{NO}_2$, may be prepared by nitrating naphthalene in acetic acid solution.

The naphthalene (5 g.) is dissolved in acetic acid (10 c.c.), nitric acid (sp. gr. 1.4; 5 g.) is added, and the solution is heated on a water-bath during about half an hour; the product which crystallises from the cold solution, is separated, washed with a little water and recrystallised from alcohol. On the large scale it is prepared by treating naphthalene with a diluted mixture of nitric and sulphuric acids.

It crystallises in yellow prisms, melts at 61° , and boils at 304° ; on oxidation with nitric acid, it yields nitrophthalic acid (p. 476).

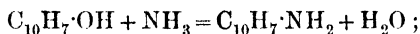
β -Nitronaphthalene is not formed by nitrating naphthalene, but it may be prepared by dissolving β -nitro- α -naphthylamine (a compound obtained by treating α -naphthylamine with dilute nitric acid) in an alcoholic solution of hydrogen chloride, adding finely divided sodium nitrite, and then heating the solution of the diazonium-compound (compare p. 401),



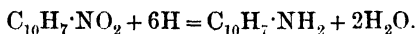
It crystallises in yellow needles, melting at 79° .

The **amino-derivatives** of naphthalene are very similar in properties to the corresponding benzene derivatives, except that even the monoamino-compounds are crystalline at ordinary temperatures. They have a neutral reaction to litmus, and yet are distinctly basic and form salts with acids; these salts, however, are hydrolysed to some extent by cold water, in which, as a rule, they are only sparingly soluble. The amino-compounds may be converted into diazonium-compounds, aminoazo-compounds, &c., by reactions similar to those employed in the case of the amino-benzenes, and many of the substances obtained in this way, as well as the amino-compounds themselves, are extensively employed in the manufacture of dyes.

α -Naphthylamine, $\text{C}_{10}\text{H}_7\cdot\text{NH}_2$, may be obtained by heating *α -naphthol* with ammonia at 250° under pressure,



it is prepared commercially by reducing *α -nitronaphthalene* with iron-filings and hydrochloric acid at about 50° ,



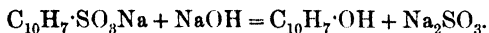
Nitronaphthalene (1 part; 10 g.) is mixed with iron borings (2 parts) in a flask, and ordinary concentrated hydrochloric acid (6.5–7 parts) is added in small quantities at a time; the flask is well shaken during the operation and the mixture is kept at about 80° . As soon as a test portion of the product is completely soluble in hot water (except for

metal or oxide), excess of alkali is added, the base is distilled in (superheated) steam, and separated on a suction-filter.

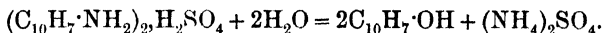
α -Naphthylamine is colourless, crystalline, melts at 50° , and boils at 300° ; it has a disagreeable smell, turns red on exposure to the air, and its salts give a blue precipitate with ferric chloride and other oxidising agents. On oxidation with a boiling solution of chromic acid, it is converted into α -naphthaquinone (p. 486) and phthalic acid. The *hydrochloride* is readily soluble in cold water, but is precipitated in crystals, even from dilute solutions, on the addition of concentrated hydrochloric acid.

β -Naphthylamine is not prepared from β -nitronaphthalene (as this substance is only obtained with difficulty, p. 483), but by heating β -naphthol with concentrated ammonia at 200° , or with ammonium sulphite and ammonia at about 160° , under pressure. It crystallises in colourless plates, melts at 112° , and boils at 294° ; it differs markedly from α -naphthylamine in being odourless, and its salts give no colouration with ferric chloride. On oxidation with potassium permanganate, it yields phthalic acid.

The two **naphthols**, or monohydroxy-derivatives of naphthalene, correspond with the monohydric phenols, and are compounds of considerable importance, as they are extensively employed in the colour industry. They both occur in coal-tar, but only in small quantities, and, therefore, are prepared by fusing the corresponding sulphonic acids with caustic soda (compare p. 485),



α -Naphthol is also manufactured from α -naphthylamine, the salts of which, *unlike* those of aniline, are decomposed by water at about 200° ,



Their properties, on the whole, are very similar to those of the phenols, and, like the latter, they dissolve in caustic alkalis, yielding metallic derivatives, which are decomposed by carbonic acid; the hydrogen of the hydroxyl-group in the naphthols may also be displaced by an acetyl- or an alkyl-group, just as in phenols, and on treatment with pentachloride or pentabromide of phosphorus, a halogen atom is substituted for the hydroxyl-group. The naphthols further resemble the phenols in giving colour reactions with ferric chloride.

In some respects, however, the naphthols differ from the phenols, inasmuch as the hydroxyl-groups in the former more readily undergo change; when, for example, a naphthol is heated with ammonia at 250° , it is converted into the corresponding amino-compound (p. 483), whereas the conversion of phenol into aniline requires a temperature of $300-350^{\circ}$, other conditions remaining the same. Again, when a naphthol is heated with an alcohol and hydrogen chloride, it is converted into its alkyl-derivative, whereas alkyl-derivatives of phenols cannot, as a rule, be obtained in this way.

α -Naphthol, $C_{10}H_7\cdot OH$, is formed when β -benzylidenepropionic acid is heated at about 300° (compare p. 463), an important synthesis, which proves that the hydroxyl-group is in the α -position; it is prepared from *α -naphthylamine*, as just mentioned, or from *naphthalene- α -sulphonic acid* (p. 486). It is a colourless, crystalline substance, melting at 94° , and boiling at 279° ; it has a faint smell, recalling that of phenol, and it dissolves freely in many organic solvents, but is only sparingly soluble in hot water. Its aqueous solution gives with ferric chloride a violet, flocculent precipitate, consisting probably of an iron compound of *α -dinaphthol*, $HO\cdot C_{10}H_6\cdot C_{10}H_6\cdot OH$, an oxidation product of the naphthol. It dissolves readily in caustic alkalis but not in solutions of alkali carbonates.

α -Naphthol, like phenol, is very readily attacked by nitric acid, and gives a *dinitro*-derivative, $C_{10}H_5(NO_2)_2\cdot OH$, which crystallises in yellow needles, melting at 138° ; its sodium derivative, $C_{10}H_5(NO_2)_2\cdot ONa, H_2O$, employed in dyeing silk, is known commercially as *Naphthol yellow*.

β -Naphthol, prepared by fusing *naphthalene- β -sulphonic acid* with caustic soda, melts at 122° , and boils at 286° ; it is a colourless, crystalline compound, readily soluble in hot water, and, like the α -derivative, it has a faint, phenol-like smell and forms readily soluble metallic derivatives with caustic alkalis. Its aqueous solution gives, with ferric chloride, a green colouration and a flocculent precipitate of *β -dinaphthol*, $HO\cdot C_{10}H_6\cdot C_{10}H_6\cdot OH$.

Sulphonic Acids.—Perhaps the most important derivatives of naphthalene, from a commercial point of view, are the various mono- and di-sulphonic acids, which are obtained from the hydrocarbon itself, from the naphthylamines, and from the naphthols, and used in large quantities in the manufacture of dyes. It would be of little use to describe individually the very numerous

compounds of this class, but some account of them may be given.

Naphthalene is readily sulphonated, yielding two *mono-sulphonic acids*, $C_{10}H_7 \cdot SO_3H$ —namely, the α - and β -compounds, both of which are formed when the hydrocarbon is heated with sulphuric acid, but the lower the temperature, the larger the proportion of the α -acid. Thus, at 80° the product consists of about 96 per cent. of the α - and 4 per cent. of the β -acid, but at 160° 15 per cent. of the α - and 85 per cent. of the β -compound are obtained. (Compare phenolsulphonic acid, p. 429.)

Naphthalene- β -sulphonic acid may be prepared in the laboratory by the following method: Naphthalene (125 g.) is heated to and kept at 160° in a wide beaker (loosely covered with a piece of cardboard) while 93 per cent. sulphuric acid (200 g.) is added in the course of about 15 minutes to the *well-stirred* liquid; about 5 minutes later, the product, having cooled a little, is very cautiously poured into water (150 c.c.), the solution is left until it has acquired room temperature, and the acid is separated on a suction-pump. The crude preparation is dissolved in one-half of its weight of boiling water, and the solution is filtered from any unchanged naphthalene or from small quantities of *di-naphthylsulphone*, $(C_{10}H_7)_2SO_2$, which are usually formed: to the filtrate concentrated hydrochloric acid (a volume equal to one-third of that of the water used) is added and the solution is cooled slowly. The β -sulphonic acid separates in lustrous scales ($3H_2O$).

Di-sulphonic acids may be obtained by strongly heating naphthalene with anhydrosulphuric acid.

Theoretically, fourteen isomeric *naphthylaminemonosulphonic acids*, $C_{10}H_6(NH_2) \cdot SO_3H$, may be obtained—namely, seven derived from α -naphthylamine, and seven from the β -base; of these compounds, thirteen seem to be known. The most important, perhaps, is *1:4-naphthylaminemonosulphonic acid*, or *naphthionic acid*, which is practically the sole product of the action of sulphuric acid on α -naphthylamine; it is crystalline, very sparingly soluble in cold water, and is used in the manufacture of Congo red and other dyes (p. 603).

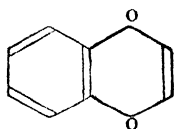
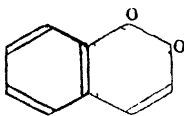
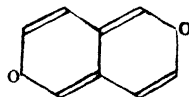
The *naphtholmonosulphonic acids* correspond in number with the naphthylaminemonosulphonic acids, and are also extensively used in the colour industry.

α -**Napthaquinone**, $C_{10}H_6O_2$, is a derivative of naphthalene, corresponding with (p-benzo)quinone, and, like the latter, it is formed when various mono- and di-substitution products of the hydrocarbon (but only those in which the substituent groups

occupy the 1 or 1:4-position) are oxidised with sodium dichromate and sulphuric acid; *α*-naphthylamine, 1:4-aminonaphthol, and 1:4-diaminonaphthalene, for example, may be employed. As a rule, however, naphthalene itself is oxidised with a boiling solution of chromic acid in acetic acid (a method not applicable for the preparation of quinone from benzene), as the product is then more easily obtained in a state of purity.

α-Naphthaquinone crystallises from alcohol in deep-yellow plates, melting at 125°; it resembles quinone in colour, in having a curious pungent smell, and in being very volatile, subliming readily even at 100°, and distilling rapidly in steam. Unlike quinone, it is not easily reduced by sulphurous acid, but some reducing agents convert it into 1:4-dihydroxynaphthalene, $C_{10}H_6(OH)_2$, just as quinone is transformed into quinol (p. 446). This close similarity in properties clearly points to a similarity in constitution, so that *α*-naphthaquinone may be represented by the formula given below.

β-Naphthaquinone, $C_{10}H_6O_2$, isomeric with the *α*-compound, is formed when *α*-amino-*β*-naphthol is oxidised with potassium dichromate and dilute sulphuric acid, or with ferric chloride; it crystallises in red needles, decomposes at about 115° without melting, and on reduction with sulphurous acid, is converted into 1:2-dihydroxynaphthalene. It differs from *α*-naphthaquinone and from quinone in colour, in having no smell, and in being non-volatile, properties which, though apparently insignificant, are of some importance, as they distinguish *ortho*-quinones from *para*-quinones; the latter are generally deep-yellow, volatile compounds, having a pungent odour, whereas the former are red, non-volatile, and odourless. *β*-Naphthaquinone is an *ortho*-quinone corresponding with *o*-benzoquinone (p. 447), and its constitution may be represented by the formula shown below:

*α*-Naphthaquinone.*β*-Naphthaquinone.

Amphi-naphthaquinone.

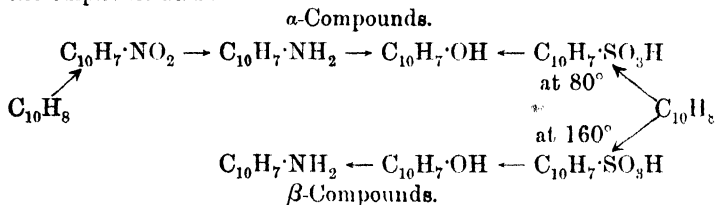
Both *α*- and *β*-naphthaquinone are oxidised by nitric acid, giving *o*-phthalic acid, a proof that in both compounds the two oxygen

atoms are united with only one nucleus ; that the one is a *para*-, the other an *ortho*-quinone, is established by their methods of formation and their conversion into compounds of known structures.¹

Amphi-naphthaquinone, $C_{10}H_6O_2$, may be represented by the formula just given in which the oxygen atoms are combined with different nuclei. It may be prepared by the oxidation of 2:6-dihydroxynaphthalene, in benzene solution, with lead dioxide. It is reddish-yellow, non-volatile, and odourless, and resembles, therefore, the *ortho*- rather than the *para*-quinones.

The above description of some of the more important naphthalene derivatives will be sufficient to show the close relationship which these compounds bear to the corresponding derivatives of benzene ; they are prepared, as a rule, by the same methods as their analogues of the benzene series, and resemble the latter closely in chemical properties ; consequently the general reactions and generic properties of benzene derivatives are met with again in the case of naphthalene compounds.

The following scheme shows how some of the more important naphthalene derivatives are produced ; it should be noted that β -naphthol and β -naphthylamine are both obtained starting from the β -sulphonic acid, but that α -naphthylamine is prepared from the nitro-compound, and α -naphthol either from this base or from the sulphonic acid :



The Orientation of Naphthalene Derivatives.

For the orientation of the mono-substitution products of naphthalene, it was necessary, as in the case of the di-derivatives of benzene (p. 343), to determine the structures of one or more compounds, which might then serve as standards. Now nitronaphthalene, the first product of the nitration of the hydrocarbon, oxidised by chromic acid, gave a nitrophthalic acid, which was proved to have the structure, $[2\text{COOH}:\text{NO}_2=1:2:3]$; the nitro-group in the nitronaphthalene must therefore be in the α -

¹ Compare foot-note, p. 447.

position. This nitronaphthalene on reduction gave a naphthylamine, which when diazotised, &c., was transformed into a naphthol; this compound, therefore, must also be an α -derivative, a conclusion which was fully confirmed by Fittig's synthesis of the same naphthol (p. 478) by simple reactions, from a compound of known constitution. These three derivatives, having thus been orientated, served as standards; any compounds obtained from, or converted into, any one of these standards by simple substitution, must belong to the α -series; a naphthalene derivative, $C_{10}H_7X$, isomeric with an α -compound, must consequently belong to the β -series.

The orientation of a di-derivative may sometimes be ascertained in a simple manner, but may be a task of considerable difficulty. In the first place the derivative is submitted to vigorous oxidation. Certain groups, such as $HO-$, and NH_2- , render the substituted nucleus more easily oxidisable, and if both are united to the same benzene nucleus that particular one is disintegrated, leaving phthalic acid. Other substituents, such as halogens or NO_2- groups, render the nucleus less readily attacked, and if both are united to the same one, a di-substituted phthalic acid is obtained. In the latter case the derivative of phthalic acid can be orientated by the usual methods, and the structure of the naphthalene derivative is thus ascertained. In the former case (and also in the latter if necessary) each of the two groups is displaced in turn by hydrogen, and it is thus found whether the compound is an $\alpha\alpha$ -, $\beta\beta$ -, or $\alpha\beta$ -derivative; if it is proved to be either $\alpha\alpha$ - or $\beta\beta$ -, its orientation is completed, but this is not so if it is an $\alpha\beta$ -di-derivative. When the results of oxidation show that the substituents are combined with *different* nuclei, it is easy to find whether they are in α - or in β -positions by displacing each in turn by hydrogen, but even if both are α - or both are β - the orientation is still incomplete. In such cases various other methods of investigation, including syntheses from substituted β benzylidenepropionic acids, must be employed, before the structures of the compounds can be established.

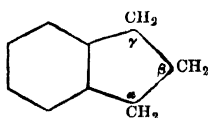
The above account will serve to indicate the principles on which the orientation of naphthalene derivatives is based. At the present time so many di-derivatives, including all the ten theoretically possible dichloronaphthalenes, have been orientated, that it may only be necessary to convert the new compound into one of these standards.

Aromatic-Aliphatic Cyclic Compounds.

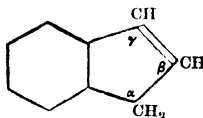
In the molecule of naphthalene both the closed-chains which are *condensed* together contain $>CH$ groups, which have an aromatic or benzenoid character. Other hydrocarbons are known in which a closed-chain having aliphatic properties is condensed with a benzene nucleus. Tetrahydronaphthalene (tetralene), for example, obtained by the reduction of naphthalene (p. 482), is

a compound of such a type; one of the closed-chains in its molecule is aromatic and shows the reactions of benzene, whereas the other contains $>\text{CH}_2$ groups, which behave like those in the molecule of a paraffin and give substitution products only with difficulty.

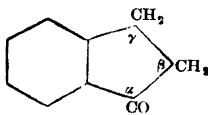
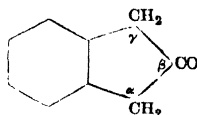
The hydrocarbon, *hydrindene*, is a lower homologue of tetrahydronaphthalene, and its molecule consists of a closed aliphatic chain of five carbon atoms *condensed* with a benzene nucleus; the structural formula of this hydrocarbon and those of some of its derivatives are given below, the letters α , β , γ , serving to show the positions of substituents:



Hydrindene.

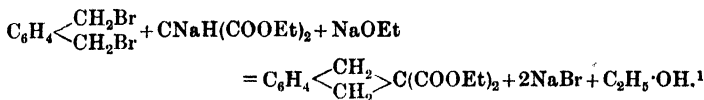


Indene.

 α -Hydrindone. β -Hydrindone.

The α - and γ -positions in hydrindene are, of course, identical, and γ -hydrindone is therefore the same as the α -compound. In the case of indene, although apparently the α -, β -, and γ -positions are all different, only two series of substitution derivatives (β - and α - or γ -) exist, because the olefinic binding readily passes from the $\alpha\beta$ - to the $\beta\gamma$ -position, or *vice versa*, with the migration of a hydrogen atom.

Hydrindene, C_9H_{10} , was first obtained by reducing coal-tar *indene* (below) with sodium and alcohol; it has been synthesised by a method which establishes its constitution: *o*-Xylylene dibromide, prepared by brominating the hydrocarbon at its boiling-point, is warmed with ethyl sodiomalonate and sodium ethoxide,



The *ethyl hydrindenedicarboxylate*, so formed, is hydrolysed,

¹ This reaction really occurs in several stages, but for the sake of brevity the changes are summarised in the one equation.

the dicarboxylic acid is converted into the monocarboxylic acid in the usual manner, and the barium salt of the *hydrindene* β -carboxylic acid is destructively distilled; indene is thus formed with the liberation of hydrogen. The indene is then reduced. Hydrindene boils at 177° and gives rise to substitution derivatives of various types by the displacement of hydrogen atoms of the benzene nucleus.

Indene, C_9H_8 , is contained in that fraction of coal-tar which is collected from 175° to 185° , and may be isolated from this product by precipitation with picric acid (p. 428); the *picrate* is purified by recrystallisation and then distilled in steam, whereby it is decomposed and indene passes over. Indene boils at 182° , and readily undergoes atmospheric oxidation; being an *olefine*, it combines directly with bromine, giving *dibromohydrindene* or *indene dibromide*, and it also combines with hydrogen (see above); when heated alone, or with hydrochloric acid, or even when it is kept at ordinary temperatures, it undergoes polymerisation and gives a resinous substance.

α -**Hydrindone**, C_9H_8O , is obtained, together with hydrogen chloride, by warming *phenylpropionyl chloride*, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot COCl$, with aluminium chloride, a reaction analogous to that by which acetophenone is produced from benzene and acetyl chloride (p. 444). It melts at 41° , boils at 244° , and forms an *oxime* (m.p. 146°); when this oxime is reduced with sodium amalgam and water, it is converted into α -**hydrindamine**, $C_9H_9 \cdot NH_2$, a *dl*-base (b.p. 220°), which may be resolved into its optically active components. When hydrindamine hydrochloride is heated alone, it decomposes into indene and ammonium chloride.

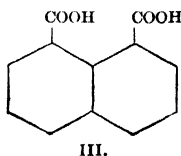
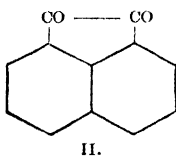
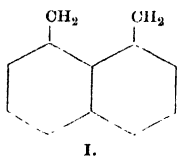
β -**Hydrindone**, C_9H_8O , is produced when the calcium salt of *phenylene-o-diacetic acid*¹ is heated, a reaction which may be compared with that by which ketones are formed from *two* molecules of a monocarboxylic acid; it melts at 61° , boils at 220 – 225° , and, like α -hydrindone, shows the ordinary reactions of a ketone.

Two **di**- and one **tri**-keto-derivatives of hydrindene are also known; the hydrate of triketohydrindene, known as *ninhydrin*, is used in testing for amino-acids and proteins (pp. 544, 575).

Acenaphthene, $C_{12}H_{10}$ (i., next page), is related to naphthalene

¹ This acid is obtained by treating *o*-xylylene dibromide (p. 372) with potassium cyanide, and hydrolysing the *o*-xylylene dicyanide which is thus formed.

in much the same way as hydrindene is related to benzene. It occurs in coal-tar, and is a component of the heavy oil (p. 326), from which, however, it is isolated only with difficulty. It crystallises in needles, melts at 95° , and boils at 278° ; on oxidation with chromic acid in glacial acetic acid solution, it is converted into *acenaphthaquinone* (II.), a yellow crystalline substance melting at 261° , which is easily oxidised further, giving *naphthalic acid* or *1:8-naphthalenedicarboxylic acid* (III.).



Naphthalic acid does not melt, but at about 180° it is converted into *naphthalic anhydride* (m.p. 266°) ; this fact shows that two carboxyl groups in the peri- or 1:8-position behave like those in the o-position in the benzene or naphthalene nucleus (compare p. 503).

CHAPTER XXXIV.

ANTHRACENE AND PHENANTHRENE.

Anthracene, $C_{14}H_{10}$, is a hydrocarbon of commercial importance, as it is the starting-point in the manufacture of alizarin, which is employed in producing Turkey-red and various other dyes ; it is prepared commercially from coal-tar. The crude mixture of hydrocarbons and other substances known as '50 per cent. anthracene' (p. 328) is treated with some solvent, such as pyridine, which extracts phenanthrene, &c., and is then distilled in superheated steam, or recrystallised from pyridine, but its isolation is very troublesome.

Anthracene crystallises from benzene in colourless, lustrous plates, which show a beautiful blue fluorescence ; it melts at 218° , boils at 340° , and dissolves freely in boiling benzene, but is only sparingly soluble in alcohol and ether. Saturated alcoholic solutions of anthracene and of picric acid, when mixed, give a precipitate of *anthracene picrate*, $C_{14}H_{10} \cdot C_6H_2(NO_2)_3 \cdot OH$, which

crystallises in ruby-red needles, melting at 138° ; this compound is resolved into its components when it is treated with a large quantity of alcohol (distinction from phenanthrene picrate, p. 501).

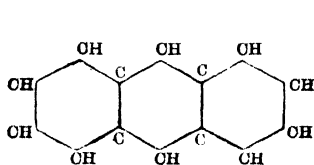
Constitution.—The molecular formula of anthracene ($C_{14}H_{10}$) suggests that this hydrocarbon is related to benzene (C_6H_6), naphthalene ($C_{10}H_8$), and other *closed-chain* compounds, rather than to hydrocarbons of the aliphatic series. The behaviour of anthracene towards chlorine and bromine is also, on the whole, similar to that of benzene and naphthalene—that is to say, anthracene yields additive or substitution products according to the conditions; moreover, towards concentrated sulphuric acid it behaves like other aromatic compounds, and is converted into sulphonic acids. When treated with nitric acid, however, instead of yielding a nitro-derivative, as might have been expected, it is oxidised to anthraquinone, $C_{14}H_8O_2$, two atoms of hydrogen being displaced by two atoms of oxygen; this change takes place even with dilute nitric acid, but under particular conditions, the concentrated acid gives (γ)-nitroanthracene, $C_{14}H_9\cdot NO_2$.

Now, the conversion of anthracene into anthraquinone is not only closely analogous to that of naphthalene, $C_{10}H_8$, into α -naphthaquinone, $C_{10}H_6O_2$ (p. 487), but is also an oxidation process of a kind (namely, the substitution of oxygen atoms for an *equal* number of hydrogen atoms) which is unknown in the case of the aliphatic hydrocarbons; anthracene, therefore, is a closed-chain compound. Another highly important fact, bearing on the constitution of anthracene, is that, although the hydrocarbon and most of its derivatives are resolved into simpler substances only with very great difficulty, when this does occur, one of the products is always some benzene derivative, usually phthalic acid.

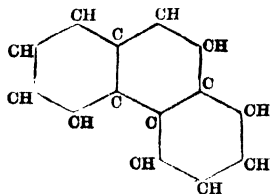
Now, if the molecule of anthracene contained only one benzene nucleus, or even if, like naphthalene, it contained two condensed benzene nuclei, there would still be certain carbon and hydrogen atoms which would have to be regarded as forming *unsaturated* side-chains; but experience has shown that even *saturated* side-chains in benzene are oxidised with comparative facility, giving carboxylic acids. Consequently, it is impossible to assume the presence of *any* side-chain in anthracene, a compound which is always oxidised to the neutral substance, anthraquinone, without loss of carbon. Arguments of this kind, therefore, lead

to the conclusion that the molecule of anthracene is composed *only* of combined or condensed nuclei; as, moreover, the hydrocarbon may be indirectly converted into phthalic acid, it must be concluded that two of these nuclei are condensed together in the *o*-position, as in naphthalene.

If, now, an attempt is made to deduce a constitutional formula for anthracene on this basis, and it is further assumed that all the closed-chains are composed of *six* carbon atoms, as in naphthalene, the following suggest themselves as alternative formulæ,



I.

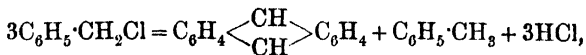


II.

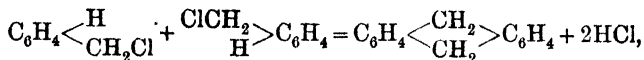
although, of course, neither could be accepted as final without further evidence.

Many facts, however, have led to the conclusion that the constitution of anthracene must be represented by the symmetrical formula I. (formula II. expressing that of phenanthrene, p. 501); this formula accounts satisfactorily for all that is known about anthracene, including a number of important syntheses of the hydrocarbon, the isomerism of its derivatives and its relation to anthraquinone.

Anthracene may be obtained synthetically in various ways from compounds of known structure. It is produced when benzyl chloride is heated with aluminium chloride,

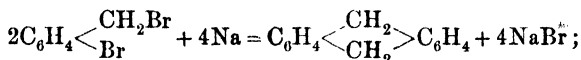


the *dihydroanthracene* (p. 496), which is formed as an intermediate product,



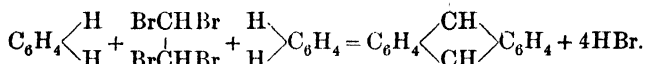
being converted into anthracene by the loss of hydrogen, which reduces part of the benzyl chloride to toluene (as expressed in the first equation). Anthracene is also formed, together with

dihydroanthracene and phenanthrene (p. 501), when *o*-bromobenzyl bromide (prepared by brominating boiling *o*-bromotoluene, $C_6H_4Br \cdot CH_3$) is treated with sodium,



here, again, *dihydroanthracene* is the primary product, and from it anthracene is formed by the loss of hydrogen.

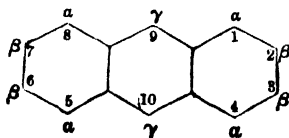
Another interesting synthesis may be mentioned—namely, the formation of anthracene when a mixture of *tetrabromoethane* and benzene is treated with aluminium chloride,



All these methods of formation are accounted for in a simple manner with the aid of the symmetrical formula, i. (p. 494).

Isomerism of Anthracene Derivatives.—Further evidence in support of this formula is afforded by the study of the isomerism of the substitution products of anthracene, although, in many cases, only a few of the isomerides theoretically possible have as yet been prepared.

By the substitution of an atom or radical for one atom of hydrogen in the molecule of anthracene, it is possible to obtain *three* (but not more than three) isomerides; this fact is readily accounted for with the aid of the given formula, which for this purpose may be numbered and lettered as shown below, the symbols, C and H, being omitted:



It will then be seen that there are three positions (α , β , γ), all of which are differently situated relatively to the rest of the molecule; these mono-substitution products are distinguished by the letters α , β , γ (or by the numerals), according to the position of the substituent. When two atoms of hydrogen are displaced by identical atoms or groups, *fifteen* isomeric di-substitution products may be obtained; these are distinguished with the aid of the numerals.

Although the symmetrical expression (p. 494) shows the framework of the anthracene molecule, a complete structural formula of the compound cannot be written, for the same reason as that given in the case of benzene (p. 336; compare also naphthalene, p. 480).

In order to avoid repetition it may be pointed out that this also applies to all aromatic substances, including those such as pyridine and quinoline (p. 504) in which a N-atom takes the place of a CH group of the nucleus; also to compounds such as furan, thiophene and pyrrole (p. 518), in which the closed chains have an aromatic or benzenoid character. The symbols by which such structures are respectively represented serve, nevertheless, the main purposes of complete formulae.

Dihydroanthracene, $C_6H_4 \begin{smallmatrix} \text{CH}_2 \\ \text{CH}_2 \end{smallmatrix} C_6H_4$, a substance of little importance, is formed when anthracene is reduced with boiling concentrated hydriodic acid, or with sodium amalgam and water. It is colourless, melts at $106-108^\circ$, and when heated with sulphuric acid it is converted into anthracene.

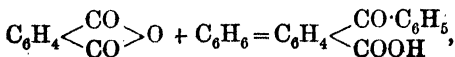
Anthracene dichloride, $C_6H_4 \begin{smallmatrix} \text{CHCl} \\ \text{CHCl} \end{smallmatrix} C_6H_4$, like dihydroanthracene, is an additive product of the hydrocarbon; it is obtained when chlorine is passed into a cold solution of anthracene in carbon disulphide, whereas at 100° substitution takes place, with formation of *γ-monochloroanthracene* and *γγ-dichloroanthracene*; these substitution products crystallise in yellow needles, melting at 103° and 209° respectively, and they are both converted into anthraquinone on oxidation, a fact which shows the positions of the chlorine atoms.

Anthraquinone, $C_6H_4 \begin{smallmatrix} \text{CO} \\ \text{CO} \end{smallmatrix} C_6H_4$, is formed, as already mentioned, when anthracene is oxidised with chromic or nitric acid.

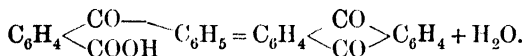
Anthracene (1 part) is dissolved in boiling glacial acetic acid (about 12 parts), and a solution of chromic acid (2 parts) in glacial acetic acid is slowly added to the boiling solution. At the end of about $1\frac{1}{2}$ hours, the solution is diluted with water, allowed to cool, and the anthraquinone is separated on a suction-filter; the product is purified by recrystallisation from acetic acid or by sublimation.

Anthraquinone is manufactured by oxidising finely divided anthracene, suspended in water, with sodium dichromate and 50 per cent. sulphuric acid. The product is collected on a filter, washed, dried, and sublimed.

Anthraquinone may be produced synthetically, and is now prepared commercially, by treating a solution of phthalic anhydride (p. 458) in benzene with aluminium chloride; *o-benzoylbenzoic acid* is first produced,

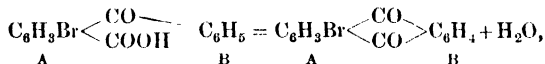


but by the further action of the aluminium chloride (or of sulphuric acid), this intermediate product is converted into anthraquinone with the loss of one molecule of water,



This synthesis proves that the molecule of anthraquinone contains two $\text{C}_6\text{H}_4 \begin{array}{c} \text{CO} \diagup \\ \text{COOH} \diagdown \end{array}$ groups, united by two $\text{CO} \begin{array}{c} \diagup \\ \diagdown \end{array}$ groups.

That the two $\text{CO} \begin{array}{c} \diagup \\ \diagdown \end{array}$ groups occupy the *o*-position in the one benzene nucleus is known, because they do so in phthalic acid; that they occupy the *o*-position in the second benzene nucleus has been proved as follows: When *bromophthalic anhydride* is treated with benzene and aluminium chloride, *bromobenzoylbenzoic acid* is produced, and this, when treated with sulphuric acid, yields *bromoanthraquinone*,



in the molecule of which the two $\text{CO} \begin{array}{c} \diagup \\ \diagdown \end{array}$ groups are known to be united to the nucleus A in the *o*-position.

Now, when bromoanthraquinone is heated with potash at 160° , it is converted into *hydroxyanthraquinone*, $\text{C}_6\text{H}_3(\text{OH}) \begin{array}{c} \text{CO} \\ \text{CO} \end{array} \text{C}_6\text{H}_4$, which,

with nitric acid, yields phthalic acid, $\begin{array}{c} \text{COOH} \\ \text{COOH} \end{array} \text{C}_6\text{H}_4$, the group A being oxidised; therefore the two $\text{CO} \begin{array}{c} \diagup \\ \diagdown \end{array}$ groups are attached to B, as well as to A, in the *o*-position, and anthraquinone has the constitution represented above, a conclusion which affords strong support to the structural formula of anthracene already given (p. 494).

Anthraquinone crystallises from glacial acetic acid in pale-yellow needles, melts at 285° , and sublimes at higher temperatures; it is very stable, and is only with difficulty attacked by oxidising agents, by sulphuric acid, or by nitric acid. When it is distilled with zinc-dust, it is converted into anthracene. It resembles the aromatic ketones much more closely than it does the *p*-quinones; it has no smell, is by no means readily volatile, and is not reduced by sulphurous acid; unlike quinone it is not an oxidising agent.

Test for Anthraquinone.—When about 0.1 g. of finely divided anthraquinone is heated with dilute caustic soda and a little zinc-dust, an intense red colouration is produced, but when shaken in contact with air, the solution is decolourised. In this reaction *oxanthranol* is formed,

and this substance dissolves in the alkali, forming a deep-red solution; on exposure to the air, however, it is oxidised to anthraquinone, which separates as a flocculent precipitate.

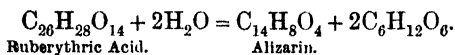
Oxanthranol, $C_6H_4 \begin{smallmatrix} \text{CO} \\ \text{CH(OH)} \end{smallmatrix} C_6H_4$, is formed by the reduction of one of the CO< groups of anthraquinone; on further reduction the other CO< group undergoes a similar change, but the product, $C_6H_4 \begin{smallmatrix} \text{CH(OH)} \\ \text{CH(OH)} \end{smallmatrix} C_6H_4$, loses one molecule of water, yielding *anthranol*, $C_6H_4 \begin{smallmatrix} \text{C(OH)} \\ \text{CH} \end{smallmatrix} C_6H_4$, which is finally reduced to *dihydroanthracene*.

Anthraquinone- β -monosulphonic acid, $C_6H_4 \begin{smallmatrix} \text{CO} \\ \text{CO} \end{smallmatrix} C_6H_3 \cdot SO_3H$, is formed, but only very slowly, when anthraquinone is heated with sulphuric acid at 250° ; with a large excess of anhydrosulphuric acid at 160 – 170° , a mixture of isomeric *disulphonic acids*, $C_{14}H_6O_2(SO_3H)_2$, is formed. The β -**mono**-sulphonic acid is of considerable importance, as its sodium salt is employed commercially for the preparation of alizarin.

Anthraquinone is heated with an equal weight of anhydrosulphuric acid (containing 50 per cent. of SO_3) in enamelled iron vessels at 160° . The product is poured into water, filtered from unchanged anthraquinone, and neutralised with soda; the sparingly soluble *sodium anthraquinone- β -monosulphonate* separates from the cold solution in glistening plates, and is collected in filter-presses. The more soluble sodium salts of the anthraquinone-disulphonic acids, which are always formed at the same time, remain in solution.

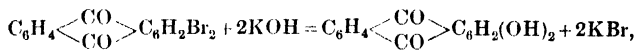
Alizarin, $C_6H_4 \begin{smallmatrix} \text{CO} \\ \text{CO} \end{smallmatrix} C_6H_2(OH)_2$, or 1:2-*dihydroxyanthraquinone*, occurs in madder (the root of *Rubia tinctorum*), a substance which has been used from the earliest times for dyeing Turkey-red, and which owes its tinctorial properties to two substances, alizarin and purpurin, both of which are present in the root in the form of glucosides.

Ruberythric acid, the glucoside of alizarin, is decomposed when it is boiled with acids, or when the madder extract is allowed to undergo fermentation, with formation of alizarin and two molecules of glucose,



A dye of such great importance as alizarin naturally attracted

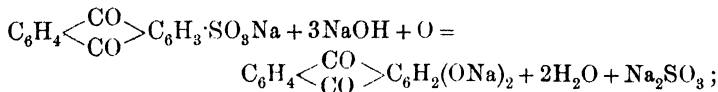
the attention of chemists, and many attempts were made to prepare it synthetically. This was first accomplished in 1868 by Graebe and Liebermann, who found that alizarin could be produced by fusing *dibromoanthraquinone*¹ with potash,



but the process was not a commercial success.

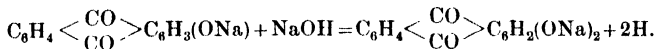
At the present day, however, madder is no longer used, and the alizarin of commerce is made from anthraquinone in the following manner, or by other synthetical methods.

Anthraquinone is converted into anthraquinone- β -sulphonic acid by the method already described (p. 498); the sodium salt of this acid is then heated with caustic soda and a little potassium chlorate, and is thus converted into the purple sodium derivative of alizarin,



from this sodium salt, alizarin is liberated with the aid of a mineral acid.

When anthraquinonesulphonic acid is fused with caustic soda, the $-\text{SO}_3\text{Na}$ group is displaced by $-\text{ONa}$ in the usual manner, but the *hydroxyanthraquinone* (sodium derivative) thus produced is further acted on by the alkali, giving alizarin (sodium derivative) and (nascent) hydrogen,



The oxidising agent (KClO_3) is added in order to prevent the nascent hydrogen from reducing the still unchanged hydroxyanthraquinone to anthraquinone.

The operation is conducted as follows: Sodium anthraquinone sulphionate (100 parts) is heated in a closed iron cylinder, fitted with a stirrer, with caustic soda (300 parts) and potassium chlorate (14 parts), during two days at 180° . The purple product is dissolved in water, the solution is filtered, if necessary, and the alizarin is precipitated with hydrochloric acid. The yellowish crystalline precipitate is collected in filter-

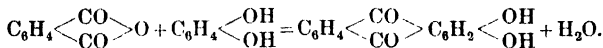
¹ Obtained by heating anthraquinone with bromine and a trace of iodine in a sealed tube at 160° . It seems uncertain whether this product is a 1:2- or a 2:3-dibromo-compound, but the hydroxyl groups in alizarin certainly occupy the 1:2-position.

presses, washed well with water, and put on the market in the form of a 10 or 20 per cent. paste. From the crude product, alizarin may be obtained in a pure state by recrystallisation from toluene, or by sublimation.

Alizarin crystallises and sublimes in dark-red prisms, which melt at 290° , and are almost insoluble in water, but moderately soluble in alcohol. It is a dihydroxy-derivative of anthraquinone, and, therefore, has the properties of a dihydric phenol; with aqueous solutions of the alkalis it forms metallic derivatives of the type, $C_6H_4 \begin{smallmatrix} \text{CO} \\ \diagup \diagdown \\ \text{CO} \end{smallmatrix} C_6H_2(OM)_2$, which are soluble in water, yielding intensely purple solutions. With acetic anhydride it gives a *diacetate*, $C_{14}H_6O_2(OAc)_2$, melting at 180° , and when distilled with zinc-dust, it is reduced to anthracene.

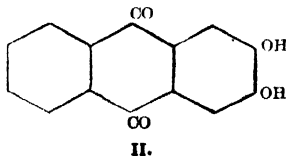
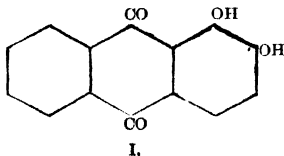
The value of alizarin as a dye is due to the fact that it yields coloured, insoluble compounds, called *lakes* (p. 582), with certain metallic hydroxides. When, for example, the purple solution of alizarin in ammonium hydroxide is added to excess of an aqueous solution of potash alum, a red lake, the basis of a complex dye, 'Turkey red,' is formed; the ferric compound, obtained in a similar manner from iron alum, is violet-black, and lakes of other colours may be prepared from other hydroxides. (Compare p. 581.)

Constitution of Alizarin.—Alizarin may be obtained by heating a mixture of phthalic anhydride and catechol with sulphuric acid at 150° ,



This reaction is clearly analogous to that by which anthraquinone is prepared from benzene (p. 496).

As catechol is *o*-dihydroxybenzene, it follows that the two hydroxyl-groups in the product must also be in the *o*-position to one another; the structure of alizarin, therefore, must be represented by one of the following formulæ:



Now, alizarin yields two isomeric *mono-nitro-derivatives*, $C_6H_4<\overset{CO}{\underset{CO}{>}}C_6H(OH)_2\cdot NO_2$, in both of which the nitro-group and the two hydroxyl-groups are combined with one and the same nucleus; its constitution, therefore, must be represented by formula I., because a substance having the constitution II. could only yield *one* such nitro-derivative.

Besides alizarin, several other *dihydroxy-* and also *trihydroxy-anthraquinones* have been obtained, but only those are of value as dyes which contain two hydroxyl-groups in the same positions as in alizarin.

Purpurin, $C_6H_4<\overset{CO}{\underset{CO}{>}}C_6H(OH)_3$, or 1:2:4-trihydroxyanthraquinone, is contained in madder, in the form of a glucoside, and may be prepared by oxidising alizarin with manganese dioxide and sulphuric acid. It crystallises in deep-red needles, melts at 253°, and gives a scarlet lake with aluminium hydroxide.

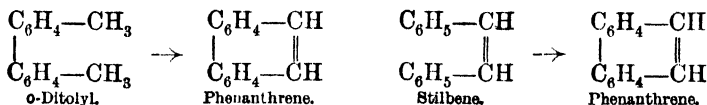
Anthrapurpurin, $HO\cdot C_6H_3<\overset{CO}{\underset{CO}{>}}C_6H_2<\overset{OH}{\underset{OH}{>}}$, or 1:2:7-trihydroxyanthraquinone, is manufactured by fusing anthraquinone-disulphonic acid, $SO_3H\cdot C_6H_3<\overset{CO}{\underset{CO}{>}}C_6H_3\cdot SO_3H$, with caustic soda and potassium chlorate (p. 499). It crystallises in yellowish-red needles, melts at 330°, and is employed in dyeing yellow shades of Turkey-red.

Many other derivatives of anthraquinone are used in dyeing (p. 594).

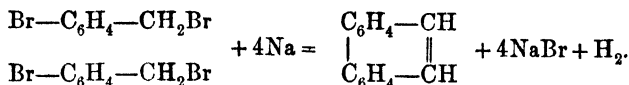
Phenanthrene, $C_{14}H_{10}$, an isomeric of anthracene, is a hydrocarbon of theoretical interest, but it has little commercial value. It occurs in considerable quantities in '50 per cent. anthracene,' from which it may be extracted with pyridine, as already described (p. 492). The resulting crude phenanthrene is converted into the picrate, which is first recrystallised from alcohol, to free it from anthracene picrate, and then decomposed by ammonia; the hydrocarbon is finally purified by recrystallisation.

Phenanthrene forms lustrous needles, melts at 101°, and distils at about 332°; it is readily soluble in many organic liquids. When oxidised with chromic acid, it is first converted into *phenanthraquinone*, $C_{14}H_8O_2$ (isomeric with anthraquinone), and then into *diphenic acid*, $C_{14}H_{10}O_4$. This acid is decomposed on distillation with soda-lime, yielding carbon dioxide and *diphenyl* (p. 370); it is, therefore, *diphenyldicarboxylic acid*, $COOH\cdot C_6H_4\cdot C_6H_4\cdot COOH$, and its formation from phenanthrene shows that the latter contains *two* benzene nuclei (p. 502).

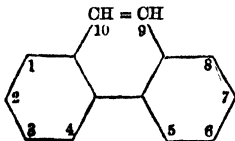
Further evidence as to the constitution of phenanthrene is obtained by studying its methods of formation. It is formed, for example, when *o*-ditolyl (prepared by treating *o*-bromotoluene with sodium) or *stilbene*¹ is passed through a red-hot tube, with the loss of hydrogen in both cases :



Phenanthrene is also produced, together with anthracene, by the action of sodium on *o*-bromobenzyl bromide (p. 495),



The facts already given and many others prove that the structure of phenanthrene may be represented as follows :²

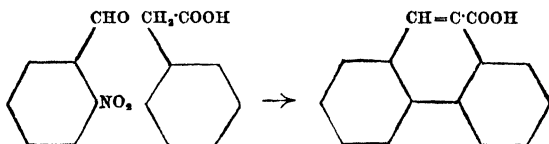


When the hydrocarbon is oxidised to phenanthraquinone, the group, $-\text{CH}=\text{CH}-$, becomes $-\text{CO}-\text{CO}-$, and on further oxidation to diphenic acid, each carbonyl-group is converted into a carboxyl-group.

Many derivatives of phenanthrene may be synthesised by an important general method (Pschorr) : *o*-Nitrobenzaldehyde is condensed with phenylacetic acid and the product is reduced to the corresponding amino-compound ; the latter is then diazotised and the diazonium salt is treated with alcohol and copper powder, which transform it into *phenanthrene-9-carboxylic acid* with the evolution of nitrogen.

¹ *Stilbene*, or *diphenylethylene*, $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{C}_6\text{H}_5$, may be prepared by treating benzaldehyde with magnesium benzyl chloride, the secondary alcohol, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{OH})\cdot\text{CH}_2\cdot\text{C}_6\text{H}_5$, which is first produced, losing a molecule of water. It crystallises in colourless prisms, melts at 124° , and, like ethylene, combines with bromine, forming *stilbene dibromide*, $\text{C}_6\text{H}_5\cdot\text{CHBr}\cdot\text{CHBr}\cdot\text{C}_6\text{H}_5$ (m.p. 237°).

² It should be noted that this formula, those just shown in the syntheses of phenanthrene, and that (II.) given on p. 494, all express the same framework (compare p. 496). The numerals serve the usual purpose and are used in the case of all substitution products.



Substituted phenylacetic acids, with at least one unoccupied *o*-position, and substituted *o*-nitrobenzaldehydes, may be used instead of the parent substances so that many phenanthrene derivatives of *known structure* may be thus prepared.

Phenanthrene may be nitrated and sulphonated; with bromine it gives an additive compound, 9:10-phenanthrene dibromide, which readily loses hydrogen bromide with the formation of 9-bromophenanthrene.

Some of the important alkaloids, such as morphine and codeine, and many other natural products (the sterols, Part III.), are derivatives of hydrophenanthrenes.

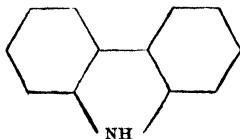
Phenanthraquinone, $\begin{array}{c} \text{C}_6\text{H}_4-\text{CO} \\ | \\ \text{C}_6\text{H}_4-\text{CO} \end{array}$, like anthraquinone, is formed

by oxidising the hydrocarbon with chromic acid. It crystallises from alcohol in orange needles, and melts at 207°. In chemical properties it shows little resemblance to *p*-benzoquinone or to α -naphthaquinone, but is more closely related to *o*-benzoquinone (p. 447), β -naphthaquinone (p. 487), and other ortho-diketones (ortho-quinones); it has no smell, and does not volatilise except when strongly heated, but it is readily reduced by sulphurous acid to 9:10-dihydroxyphenanthrene, $\text{C}_{14}\text{H}_8(\text{OH})_2$, and it combines with sodium bisulphite, forming a soluble *bisulphite* compound, $\text{C}_{14}\text{H}_8\text{O}_2, \text{NaHSO}_3, 2\text{H}_2\text{O}$; with hydroxylamine it yields a *dioxime*, $\text{C}_{14}\text{H}_8(\text{:N}\cdot\text{OH})_2$.

Diphenic acid, $\begin{array}{c} \text{C}_6\text{H}_4-\text{COOH} \\ | \\ \text{C}_6\text{H}_4-\text{COOH} \end{array}$, obtained by the oxidation of phenanthrene or phenanthraquinone (p. 501) crystallises in needles, and melts at 229°. When heated with acetic anhydride it is converted into *diphenic anhydride*, $\text{C}_{12}\text{H}_8\text{<}\begin{array}{c} \text{CO} \\ \diagup \quad \diagdown \\ \text{CO} \end{array}\text{>O}$ (m.p. 217°).

This fact is noteworthy, because it shows that anhydride formation may occur, as in the case of 1:3-naphthalenedicarboxylic acid (p. 492), even when the two carboxyl-groups are united with *different* nuclei.

Carbazole, $C_{12}H_9N$, occurs in the crude anthracene obtained from coal tar. It is colourless, melts at 238° , and forms a potassium derivative, $C_{12}H_8NK$, when it is strongly heated with potash; it is used in making dyes. Its constitution is represented by the following formula:



CHAPTER XXXV.

PYRIDINE, QUINOLINE, ISOQUINOLINE, AND OTHER HETEROCYCLIC COMPOUNDS.

Pyridine, *quinoline*, and *isoquinoline* are three closely related aromatic bases, which, together with their numerous derivatives, form a group of great theoretical interest; many of these derivatives occur in nature, and belong to the well-known and important class of compounds termed the 'vegetable alkaloids.' Pyridine derivatives are obtained by the oxidation of conine (p. 529) and nicotine (p. 530). *Quinoline* was first produced by fusing quinine and cinchonine (p. 537) with potash; it is also formed from strychnine (p. 540) under these conditions. *Isoquinoline* was first obtained from coal-tar; derivatives of this base are formed when the alkaloids *papaverine*, *narcotine* (p. 541), &c. are fused with potash.

Coal-tar, though consisting principally of hydrocarbons and phenols, contains small quantities of *pyridine* and its homologues; also *quinoline*, *isoquinoline*, and numerous other basic substances, such as aniline. The pyridine bases are dissolved, in the form of their sulphates, in the purification of the 'light oil,' by treatment with dilute sulphuric acid (p. 327), and when the dark acid liquor is afterwards treated with excess of caustic soda, they separate again at the surface of the liquid in the form of a dark-brown oil. By repeated fractional distillation, a partial separation of the various components of this oil may be effected, and crude pyridine may be obtained; by the crystallisation of their salts, or by other

methods, the pyridine and some of its homologues may be prepared in a state of purity.

A less important source of these compounds is *bone-tar* or *bone-oil*, a dark-brown, unpleasant smelling liquid formed during the dry distillation of bones, in the preparation of bone-black (animal charcoal); this oil contains considerable quantities of *pyridine* and *quinoline*, and their homologues, as well as other compounds such as *pyrrole* (p. 520). Bone-oil, purified by distillation, was formerly used in medicine under the name of *Dippel's oil*.

Pyridine and its Derivatives.

Pyridine, C_5H_5N , is formed during the destructive distillation of various nitrogenous organic substances; hence its presence in coal-tar and in bone-oil. It was discovered in bone-oil by Anderson in 1846.

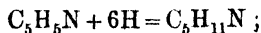
Pure pyridine, free from its homologues, may be prepared by distilling *nicotinic acid* (p. 511), or other pyridinecarboxylic acids, with soda-lime, just as pure benzene may be prepared from benzoic and phthalic acids in a similar manner.

For commercial purposes it is usually obtained from coal-tar as already described; the crude product consists mainly of pyridine, mixed with its mono- and di-methyl derivatives, and is principally used as a solvent and in 'denaturing' alcohol, in the preparation of methylated spirit.

Pyridine is formed when a mixture of acetylene and hydrogen cyanide is passed through a red-hot tube, $2C_2H_2 + HCN = C_5H_5N$, but no satisfactory synthesis is known; many pyridine derivatives, however, have been obtained from aliphatic compounds (p. 510).

Pyridine is a colourless, mobile liquid of sp. gr. 1.003 at 0° ; it boils at 115° , is miscible with water in all proportions, and possesses a pungent and very characteristic odour. It is a particularly stable substance, as it is not attacked by boiling nitric acid, or by aqueous solutions of chromic acid or potassium permanganate; with halogens, and sulphuric acid, it gives *substitution* products, such as *monobromopyridine*, C_5H_4BrN , and *pyridine-sulphonic acid*, $C_5H_4(SO_3H)N$, but only with great difficulty.

Pyridine is readily reduced by *anhydrous* alcohol and sodium giving *piperidine* or *hexahydropyridine* (p. 509),



in the presence of water, however, the nitrogen atom is eliminated, as ammonia, and *glutardialdehyde*, $\text{CHO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CHO}$, is formed. When pyridine is heated with hydriodic acid at 300° , it gives pentane and ammonia.

Pyridine is a strong base; like the aliphatic amines, it turns red litmus blue, and forms stable crystalline salts, such as the *hydrochloride*, $\text{C}_5\text{H}_5\text{N}\cdot\text{HCl}$, and the *sulphate*, $(\text{C}_5\text{H}_5\text{N})_2\cdot\text{H}_2\text{SO}_4$. The *platinichloride*, $(\text{C}_5\text{H}_5\text{N})_2\cdot\text{H}_2\text{PtCl}_6$, forms orange-yellow crystals melting at 240° , and is sparingly soluble in cold water; the *ferrocyanide* is also sparingly soluble and may serve for the purification of the crude base.

Pyridine combines directly with methyl iodide (1 mol.) with the development of heat, giving an additive product, *methylpyridonium iodide*, or *pyridine methiodide*, $\text{C}_5\text{H}_5\text{N}\cdot\text{CH}_3\text{I}$, which crystallises from alcohol, melts at 117° , and has the properties of a quaternary ammonium salt.

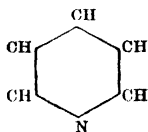
When methylpyridonium iodide is heated alone at 300° it undergoes isomeric change, and is converted into α - (and γ -) methylpyridine hydriodide; other alkyl halogen additive products show a similar behaviour, and the change is analogous to that which occurs in the case of the alkylanilines (p. 396).

Constitution.—The fact that pyridine is a strong base suggests some relation to the *amines*. It is, however, not a primary amine, because it does not give the carbylamine reaction; nor is it a secondary amine, because it does not react with nitrous acid; the necessary conclusion that pyridine is a *tertiary* base is further borne out by its behaviour towards methyl iodide. But since pyridine has the molecular formula, $\text{C}_5\text{H}_5\text{N}$, it is most improbable that it is an *open-chain* tertiary amine, because such a compound would be highly unsaturated, and readily oxidised and resolved into simpler substances. The grounds for concluding that pyridine is not an unsaturated aliphatic amine are, in fact, much the same as those which led to the conclusion that the constitution of benzene is totally different from that of dipropargyl (p. 333).

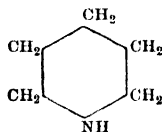
If now the properties of pyridine are compared with those of aromatic compounds, a general analogy is at once apparent; in spite of its great stability, pyridine shows, under certain conditions, the behaviour of an unsaturated compound, and, like

benzene, naphthalene, and other closed-chain compounds, yields *additive* products, such as *piperidine* (p. 509).

Considerations such as these led Körner, in 1869, to suggest that pyridine, like benzene, contains a closed-chain or nucleus, as represented by the formula (I.) given below, and this view has since been confirmed in a great many ways, notably in the following manner: Piperidine, or hexahydropyridine, the compound which is formed by the reduction of pyridine, and which is reconverted into the latter on oxidation with sulphuric acid has been prepared synthetically by a simple method (p. 509) which shows it to have the constitution (II.); pyridine, therefore, must be represented by (I.), the relation between the two compounds being the same as that between benzene and hexahydrobenzene (p. 358)



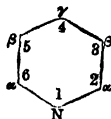
Pyridine (I.).



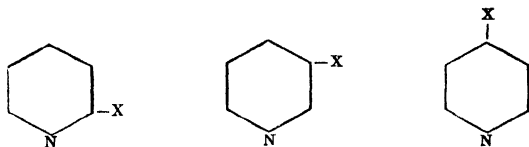
Piperidine (II.).

This conclusion is fully confirmed by a study of the isomerism of pyridine derivatives; also, from its relation to quinoline (p. 513), pyridine must be regarded as derived from benzene by the substitution of a trivalent nitrogen atom, $N\lessdot$, for one of the $CH\lessdot$ groups.

Isomerism of Pyridine Derivatives.—The *mono*-substitution products of pyridine, as, for example, the *methylpyridines*, exist in *three* isomeric forms; this fact is clearly accounted for if the framework of the parent substance is represented by a hexagon, showing the symbol for nitrogen *only* and numbered or lettered for the usual purposes:

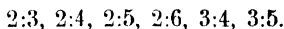


Since a *mono*-substitution product may be formed by the displacement of any one of the five hydrogen atoms, the following *three*, but not more than three, isomerides may be obtained:



The positions α and α' are identical, and so also are the positions β and β' , but the position γ is different from any of the others; the letters are generally used instead of numerals to distinguish the *mono*-substitution products.

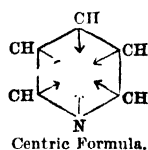
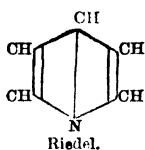
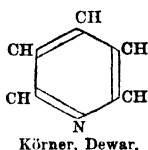
The *di*-substitution products, $C_5H_3X_2N$, exist in *six* isomeric forms, the positions of the substituents in the several isomerides being as follows,



All other positions are identical with one of these; 2:3, for example, is the same as 5:6, and 3:4 is identical with 4:5.

As regards the isomerism of its derivatives, pyridine may be conveniently compared with a *mono*-substitution product of benzene—*aniline*, for example—the effect of substituting a nitrogen atom for one of the $CH\leq$ groups in benzene being the same, in this connection, as that of displacing one of the hydrogen atoms by some substituent.

Three complete structural formulæ for pyridine have been suggested in the past and are shown below,



but according to present views (pp. 336, 480, 496) the symbol, I., on p. 507, though incomplete, is to be preferred.

Compounds, such as pyridine, in which the atoms linked together to form the closed-chain are not all the same, are classed as *heterocyclic*; those in which all such atoms are identical are *homocyclic*. In the latter case, when the closed-chain is composed of carbon atoms, the compound is classed as *carbocyclic*. There are many different types of homocyclic and of heterocyclic compounds; one or more atoms of nitrogen, oxygen, sulphur, &c., may be links of the heterocyclic systems.

Piperidine, $C_5H_{11}N$ (hexahydropyridine), is formed, as already stated, when pyridine is reduced with sodium and alcohol; it may be prepared from pepper, which contains the alkaloid, *piperine* (p. 532), a substance which is decomposed by boiling alkalis yielding piperidine and piperic acid.

Piperidine is a colourless liquid, boiling at 106° , and is miscible with water; it has a very penetrating unpleasant odour. Like pyridine, it is a strong base, turns red litmus blue, and combines with acids forming stable, crystalline salts. When heated with concentrated sulphuric acid at 300° , or with nitrobenzene at 260° , it undergoes oxidation, with the loss of six atoms of hydrogen, and is converted into pyridine.

Piperidine is a *secondary aliphatic amine* and, with nitrous acid, it yields *nitroso-piperidine*, $C_5H_{10}N\cdot NO$, an oil, boiling at 218° ; like secondary amines, moreover, it reacts with methyl iodide, giving *N-methylpiperidine hydriodide*,¹ $C_5H_{10}N\cdot CH_3\cdot HI$, and with acid chlorides, giving substituted amides, $C_5H_{10}N\cdot CO\cdot R$.

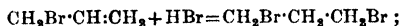
The important synthesis, already referred to, which establishes the constitution of piperidine, and also that of pyridine, was accomplished by Ladenburg in the following way: *Trimethylene dibromide*² is heated with potassium cyanide in alcoholic solution, and is thus converted into *trimethylene dicyanide*,

$Br\cdot CH_2\cdot CH_2\cdot CH_2\cdot Br + 2KCN = CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CN + 2KBr$,
which, on reduction with sodium and alcohol, yields *pentamethylenediamine*, just as methyl cyanide under similar conditions yields ethylamine,

$CN\cdot CH_2\cdot CH_2\cdot CH_2\cdot CN + 8H = NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot NH_2$;
during this reduction process some of the pentamethylenediamine is decomposed into piperidine and ammonia, and the same change

¹ The letter N before the name of the substituent signifies that the latter is directly combined with the nitrogen atom.

² *Trimethylene dibromide*, $C_3H_6Br_2$, is prepared by treating allyl bromide (p. 232) with concentrated hydrobromic acid at 0° ,

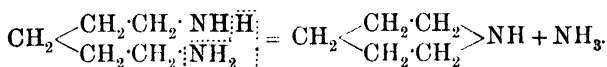


it is a heavy, colourless oil, and boils at 164° .

Since allyl bromide may be obtained from glycerol, which may be prepared from its elements (p. 220), a *complete synthesis* of piperidine may be effected.

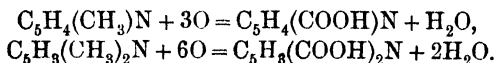
Trimethylene dibromide may also be obtained by treating trimethylene glycol (p. 219) with hydrobromic acid.

occurs, but much more completely, when the hydrochloride of the diamine is distilled,



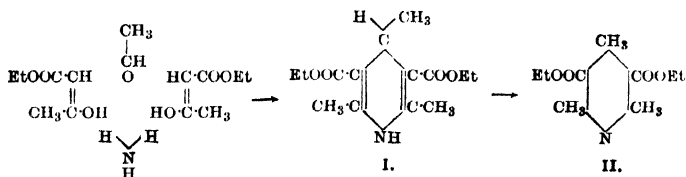
Piperidine may be reconverted into an open-chain compound in various ways. When, for example, N-benzoylpiperidine is treated with phosphorus pentachloride, it is converted into a dichloro compound, $\text{CH}_2\text{Cl} \cdot [\text{CH}_2]_4 \cdot \text{N} \cdot \text{CCl} \cdot \text{C}_6\text{H}_5$, which decomposes when it is distilled, giving 1:5-dichloropentane, $\text{CH}_2\text{Cl} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2\text{Cl}$, and benzonitrile.

Derivatives of Pyridine.—The *alkyl*-derivatives of pyridine occur in coal-tar and bone-oil, and, therefore, are present in the basic mixture obtained from the ‘light-oil’ (p. 327) in the manner already mentioned; they can only be isolated by repeated fractional distillation and subsequent crystallisation of their salts. The three (α , β , γ) isomeric *methypyridines* or *picolines*, $\text{C}_5\text{H}_4(\text{CH}_3)\text{N}$, the six isomeric *dimethypyridines* or *lutidines*, $\text{C}_6\text{H}_3(\text{CH}_3)_2\text{N}$, and the six *trimethypyridines* or *collidines*, $\text{C}_6\text{H}_2(\text{CH}_3)_3\text{N}$, resemble the parent base in most ordinary properties; unlike the latter, however, they undergo oxidation more or less readily on treatment with a solution of potassium permanganate, and are converted into *pyridinecarboxylic acids*, just as the homologues of benzene yield benzenecarboxylic acids, the alkyl-groups or side-chains being oxidised to carboxyl-groups,



This behaviour has been of great use for the determination of the positions of the alkyl-groups in many homologues of pyridine, that is to say, for their *orientation* (p. 343); the carboxylic acids into which they are converted are easily isolated and identified by their melting-points and other properties, and their constitutions have been determined in a simple manner (p. 512).

Although pyridine itself is not easily synthesised, many of its derivatives have been obtained by the *condensation* of aldehydes with esters of β -ketonic acids (p. 191) in the presence of ammonia (Hantzsch). Acetaldehyde, ethyl acetoacetate, and ammonia, for example, give *ethyl dihydrocollidinedicarboxylate* (I.), which on oxidation is converted into *ethyl collidinedicarboxylate* (II.). When the acid, obtained by hydrolysing this ester is heated with soda-lime, it is converted into 2:4:6-*trimethypyridine* (or *collidine*).



Since other aldehydes may be used instead of acetaldehyde, and various diketones in the place of (one molecule of) ethyl acetoacetate, it is possible to synthesise many derivatives of pyridine in a similar manner.

The *pyridinecarboxylic acids*, as a class, are perhaps the most important derivatives of pyridine, chiefly because they are obtained as oxidation products of some of the alkaloids.

The three (α , β , γ) *monocarboxylic acids* may be prepared by oxidising the corresponding *picolines* or *methylpyridines* (see above) with potassium permanganate. The α -carboxylic acid is usually known as **picolinic acid** (m.p. 136°), because it was first prepared from α -picoline, whereas the β -compound is called **nicotinic acid** (m.p. 229°), because it was first obtained by the oxidation of nicotine (p. 530). The third isomeride—namely, the γ -carboxylic acid—is called **isonicotinic acid**, and is the oxidation product of γ -picoline: when it is heated it sublimes without melting.

These monocarboxylic acids are all crystalline and soluble in water; they have both basic and acidic properties, and form salts with mineral acids as well as with bases, a behaviour which is similar to that of glycine (p. 202).

The α -carboxylic acid, and many other pyridinecarboxylic acids which contain a carboxyl-group in the α -position (but only such), give a red or yellowish-red colouration with ferrous sulphate. A carboxyl-group in the α -position, moreover, is usually very readily eliminated when the acid is heated; picolinic acid, for example, is much more readily converted into pyridine than is nicotinic or isonicotinic acid.

Quinolinic acid, $\text{C}_5\text{H}_3(\text{COOH})_2\text{N}$ (*pyridine-2:3-dicarboxylic acid*), is produced by the oxidation of quinoline with potassium permanganate. It crystallises in colourless prisms, is only sparingly

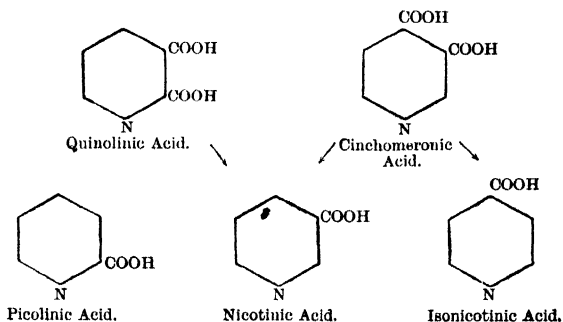
soluble in water, and gives, with ferrous sulphate, an orange colouration, one of the carboxyl-groups being in the α -position. When heated at 190° , it decomposes into carbon dioxide and nicotinic acid; on distillation with lime, quinolinic acid, like *all* pyridinecarboxylic acids, is converted into pyridine.

Unlike phthalic acid, quinolinic acid is not converted into its anhydride when it is heated alone; nevertheless, when heated with acetic anhydride, quinolinic acid gives a crystalline *anhydride*,

$C_5H_3N < \begin{smallmatrix} CO \\ CO \end{smallmatrix} > O$, melting at 134° . This fact indicates that the carboxyl-groups are in the *o*-position, as in phthalic acid; the formation of the acid from quinoline (p. 514) confirms this indication, and fully establishes the structure of the acid.

Cinchomeric acid, $C_5H_3(COOH)_2N$ (*pyridine-3-4-dicarboxylic acid*), is produced by the oxidation of quinine (p. 537) with nitric acid, or of isoquinoline with potassium permanganate; it melts at about 266° , and when cautiously heated it is decomposed into nicotinic acid, isonicotinic acid, and carbon dioxide.

Since the constitutions of quinolinic and cinchomeric acids are proved by their methods of formation, the fact that nicotinic acid is obtained from *both* these acids, which are 2:3 and 3:4 derivatives respectively, proves that nicotinic acid is pyridine-3-carboxylic acid; isonicotinic acid which is also formed from the 3:4-acid, must therefore be pyridine-4-carboxylic acid; and the third isomeric, picolinic acid, pyridine-2-carboxylic acid. It should be noted that the α , β , and γ correspond with the 2, 3, and 4 positions respectively.



Quinoline and Isoquinoline.

Quinoline, C_9H_7N , was first obtained by Gerhardt in 1842 by heating quinine with alkalis. It occurs, together with *isoquinoline*, in that fraction of coal-tar and bone-oil bases (p. 505) which is collected between 236° and 243° ; it is difficult, however, to obtain the pure substance from this mixture. On the other hand, quinoline is easily prepared synthetically by *Skraup's reaction*—namely, by heating a mixture of aniline and glycerol with sulphuric acid, together with arsenic acid or nitrobenzene, both of which act as oxidising agents.

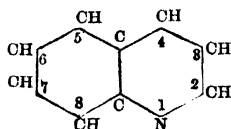
Concentrated sulphuric acid (72 g.) is gradually added to a mixture of aniline (25 g.), arsenic acid (38 g.), and anhydrous glycerol (77 g.), and the mixture is then *very cautiously* heated in a large flask (with air condenser) on a sand-bath.¹ When the reaction which first sets in has subsided, the liquid is boiled during about two and a half hours. It is then diluted with water, and treated with an excess of caustic soda to liberate the quinoline and the unchanged aniline from their sulphates; the bases are then obtained from the mixture by distillation in steam. As these two bases cannot be completely separated by fractional distillation, the whole of the aqueous distillate is acidified with sulphuric acid, and sodium nitrite is added until nitrous acid is permanently present (p. 403); the solution is then heated in order to convert the diazonium-salt into phenol, rendered alkaline with caustic soda (in order to 'fix' the phenol), and again submitted to distillation in steam. The quinoline is finally separated with the aid of a tap-funnel, dried over solid potash, and purified by fractional distillation.

Quinoline is a colourless, highly refractive oil, of sp. gr. 1.095 at 20° , and boils at 239° . It has a pleasant, characteristic smell, and is sparingly soluble in water. It forms crystalline salts, such as the *hydrochloride*, $C_9H_7N \cdot HCl$, and the *sulphate*, $(C_9H_7N)_2 \cdot H_2SO_4$, which, as a rule, are readily soluble in water. The *dichromate*, $(C_9H_7N)_2 \cdot H_2Cr_2O_7$, prepared by adding potassium dichromate to quinoline hydrochloride in aqueous solution, crystallises from water, in which it is only sparingly soluble, in glistening yellow needles, melting at 165° . The *platinichloride*, $(C_9H_7N)_2 \cdot H_2PtCl_6 \cdot 2H_2O$, is only very sparingly soluble in water.

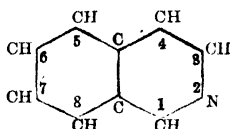
Constitution.—Quinoline is alkaline to litmus, but it does not

¹ The reaction is liable to be very vigorous, especially when nitrobenzene is used and, as soon as it starts, the burner is temporarily withdrawn.

give the reactions of a primary or those of a secondary base ; on the other hand, it combines with methyl iodide to form the additive product *methylquinolonium iodide* (*quinoline methiodide*), C_9H_7N, CH_3I , m.p. 133° , and in this and other respects shows the behaviour of a *tertiary* base (p. 518). Now the relation between pyridine, C_5H_5N , and quinoline, C_9H_7N , on the one hand, is much the same as that between benzene, C_6H_6 , and naphthalene, $C_{10}H_8$, on the other, both as regards molecular composition (the difference being C_4H_2 in both cases) and chemical behaviour ; possibly, therefore, quinoline is derived from pyridine, just as naphthalene is derived from benzene ; if so, its constitution would be expressed by one of the following formulæ :



I.



II.

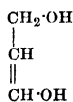
Now, quinoline differs from pyridine, just as naphthalene differs from benzene, in being relatively easily oxidised, and when heated with an alkaline solution of potassium permanganate it yields *quinolinic acid*, $C_5H_3(COOH)_2N$, a derivative of pyridine (p. 511). This fact proves that the molecule of quinoline contains a pyridine nucleus ; but it also contains a benzene nucleus, as is shown by its formation from aniline by Skraup's method. Its constitution, therefore, must be expressed by *one* of the above formulæ, as these facts admit of no other interpretation. But formula II. is inadmissible, because it does not account for the formation of quinoline from aniline. For these and many other reasons, the framework of the quinoline molecule is represented by I. (and that of isoquinoline by II. ; compare p. 517).

This symbol, or formula, although incomplete, shows clearly that quinoline is related both to benzene and to pyridine in structure and, therefore, in chemical behaviour ; with its aid many syntheses of quinoline and its derivatives⁹ have been suggested and accomplished. It also explains the observed isomerism of quinoline derivatives, and shows, for example, that *seven* mono-substitution products, $X \cdot C_9H_6N$, should exist, as has been proved to be true in the case of the *methylquinolines*.

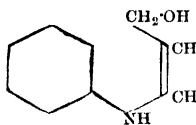
The relationship between these isomerides is plainly seen when the framework of the parent base is represented by a double hexagon, showing the symbol for nitrogen only, and numbered (as on p. 514) for the usual purpose.

Several complete structural formulæ for quinoline, differing in much the same way as those of benzene (p. 335), naphthalene (p. 480) and pyridine (p. 508), have been suggested in days gone by, but need not be given here.

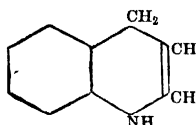
The formation of quinoline from aniline and glycerol by Skraup's reaction involves, no doubt, a series of changes, the exact nature of which is unknown. It may be that from glycerol, by the loss of a molecule of water, there is formed a compound (I.), which *condenses* with aniline to form an intermediate product (II.); the latter, by the loss of a molecule of water, may then be converted into a *dihydroquinoline* (III.), which is finally oxidised to quinoline. Various other explanations of the *mechanism* of this reaction have been suggested, but the matter is still undecided.



I.



II.

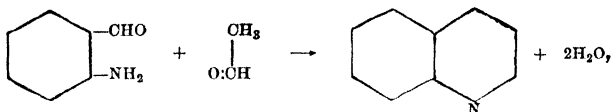


III.

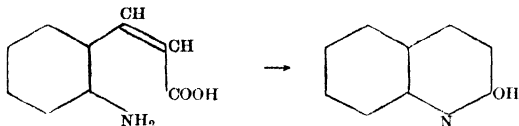
Many derivatives of quinoline may be obtained by Skraup's reaction, using substitution products of aniline, in which one at least of the *o*-positions to the NH_2 -group is not occupied; when, for example, any one of the three toluidines (p. 394) is employed, a *methylquinoline* is formed, and it is known that the product is a **Bz**-methylquinoline, that is to say, that the methyl-group is combined with carbon of the benzene nucleus; further, the constitutions of the compounds obtained from *o*- and *p*-toluidine respectively are completely established, whereas in the case of *m*-toluidine, which gives *two* products, it is known that one of these is 5- and the other is 7-methylquinoline. Other **Bz**-derivatives of quinoline may be obtained in a similar manner, and Skraup's reaction may also be used for the preparation of analogues of quinoline from the naphthylamines and other aromatic amino-compounds.

Quinoline may also be obtained synthetically by other reactions

which establish its molecular framework. It is formed when *o*-aminobenzaldehyde is condensed with acetaldehyde in the presence of dilute alkali,



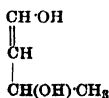
and when the vapour of allylaniline, $C_6H_5 \cdot NH \cdot CH_2 \cdot CH : CH_2$, is passed over strongly heated lead oxide. Its hydroxy-derivative (*carbostyryl*) is produced by the reduction of *o*-nitrocinnamic acid (p. 464), which is first converted into *o*-aminocinnamic acid, and then by the loss of the elements of water, into 2-hydroxyquinoline,



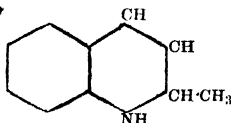
Since the carbonyl-group of a carboxylic acid does not condense with an amino-group to form $-N=C(OH)-$ it may be assumed that the *o*-aminocinnamic acid is first converted into its *lactam*, $-NH-CO-$, which then by tautomeric change gives the *lactim*, $-N=C(OH)-$. When the hydroxyquinoline is treated with phosphorus pentachloride it gives *α-chloroquinoline*, which is reduced by hydriodic acid and converted into quinoline.

Many derivatives of quinoline are obtained by the condensation of aniline (or of substitution products of aniline) with aldehydes in the presence of sulphuric acid (Döbner and Miller); aniline and acetaldehyde, for example, give 2-methylquinoline (*quinaldine*), a base (b.p. 247°), which on reduction with sodium and alcohol is transformed into di-tetrahydroquinaldine, $C_6H_4 \begin{smallmatrix} CH_2 - CH_2 \\ | \quad | \\ NH \cdot CHMe \end{smallmatrix}$ (b.p. 247°).

The *mechanism* of the formation of quinaldine is not known; it is possible that the acetaldehyde is first converted into aldol, which then undergoes a tautomeric change giving the dihydroxy-compound I.; the latter by condensation with the aniline might then give the intermediate product II., which is oxidised by the sulphuric acid to 2-methylquinoline:



I.

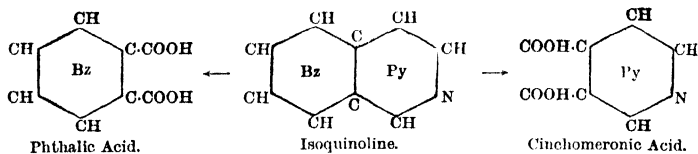


II.

Certain derivatives of quinoline and quinaldine are used for rendering photographic plates or films more sensitive to the green, yellow, or red rays of the spectrum.

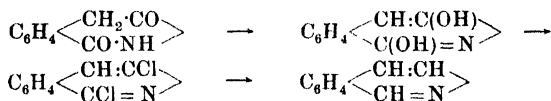
Isoquinoline, C_9H_7N , occurs in coal-tar quinoline, and may be isolated by converting the mixed bases of the fraction boiling at $236-243^\circ$ into the hydrogen sulphates, C_9H_7N, H_2SO_4 , and recrystallising these salts from alcohol (88 per cent.) until the crystals melt at 205° . The sulphate of isoquinoline, thus obtained, is decomposed with alkali, and the base purified by distillation. Isoquinoline melts at 23° , and boils at 241° ; it is a tertiary base, very like quinoline in chemical properties, and gives a crystalline *methylisoquinolonium iodide*, C_9H_7N, MeI (m.p. 159°).

The close relationship between quinoline and isoquinoline indicates that the molecule of the latter, like that of quinoline, is composed of a benzene and a pyridine nucleus condensed together. This view is confirmed by the fact that when isoquinoline is oxidised with permanganate, it yields phthalic acid together with *cinchomeronic acid*, $C_5H_3(COOH)_2N$, which is known to be a pyridinedicarboxylic acid (p. 512). If now the constitution of isoquinoline is expressed by the formula given below, these results are easily explained; oxidation takes place in two directions, in the one case the pyridine (Py), in the other the benzene (Bz), nucleus being disintegrated:



This view of the constitution of isoquinoline is fully established by the following synthesis of the base: *o*-Nitrotoluene (p. 385) is converted into *o*-cyanotoluene (*o*-tolunitrile) by methods corresponding with those employed in preparing phenyl cyanide from nitrobenzene (p. 404), and this cyano-derivative is then chlorinated at its boiling-point. The product (*o*-cyanobenzyl chloride), $CN \cdot C_6H_4 \cdot CH_2Cl$, is treated with potassium cyanide, and the *o*-cyanobenzyl cyanide, $CN \cdot C_6H_4 \cdot CH_2 \cdot CN$, is transformed into *o*-homophthalic acid, $COOH \cdot C_6H_4 \cdot CH_2 \cdot COOH$ (a homologue of phthalic acid), by hydrolysis. *Homophthalimide*, $C_6H_4 \cdot \begin{smallmatrix} CH_2 \cdot CO \\ CO \cdot NH \end{smallmatrix}$, prepared by heating the ammonium salt of the acid (compare p. 458), may be directly converted into isoquinoline by distillation over strongly

heated zinc-dust. This change may also be brought about by treating the homophthalimide with phosphorus oxychloride and then reducing the product (*dichloroisoquinoline*) with hydriodic acid; these reactions may be summarised as follows:



Cyclic bases.—It will be seen from the above description of piperidine, pyridine, and quinoline that aromatic bases which owe their basic character to the group, >NH , or >N , forming part of a closed-chain, show the same chemical behaviour as open-chain, secondary or tertiary bases respectively, so far as these particular groups are concerned.

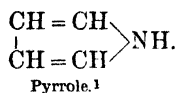
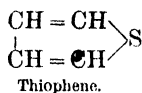
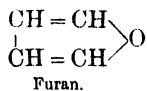
The *secondary* bases, such as piperidine, which contain the >NH group, yield *nitrosoamines*, and with an alkyl halide, they are converted into N-alkyl-substitution products, just as diethylamine, for example, reacts with ethyl iodide, giving triethylamine.

These alkyl-derivatives of the secondary closed-chain compounds are themselves tertiary bases, and with alkyl halides, form *additive* products which are quarternary ammonium salts (p. 197). The hydrogen atom of the >NH group in secondary closed-chain bases is also displaceable by the acetyl and other acyl radicals.

The *tertiary* bases, such as pyridine and quinoline, in which the nitrogen atom is not directly united with hydrogen, do not yield nitroso- or acetyl-derivatives, but they unite with one molecule of an alkyl halogen compound giving *additive* compounds, which are quaternary ammonium salts.

Furan, Thiophene, and Pyrrole.

Furan, thiophene, and pyrrole are three *heterocyclic* compounds (p. 507), the structures of which may be respectively represented by the following formulæ:



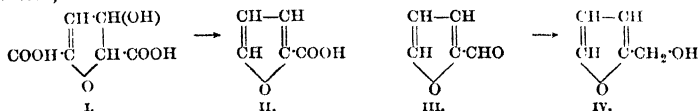
¹ The names 'furan' and 'pyrrole' are misleading, since the termination *an* suggests *ane*, which denotes a saturated hydrocarbon, and *ole* suggests an ether, such as anisole (p. 426); furfuraldehyde is sometimes called furfuro! or furol, which are also unsatisfactory names for an aldehyde.

Each is the parent substance of many derivatives, which in some ways behave like aliphatic, and in others like aromatic, compounds, and thus form connecting links between the two types.

Furan, C_4H_4O , is obtained by heating the barium salt of pyromucic acid with soda-lime (Limpriht); it is a colourless liquid, boiling at 32° and occurs in wood-tar.

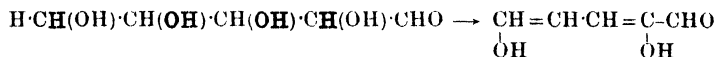
Pyromucic acid, $C_4H_3O \cdot COOH$ (*furancarboxylic acid*), is prepared by oxidising furfuraldehyde with sodium chlorate in the presence of a trace of vanadium pentoxide, but was first obtained by heating mucic acid (p. 288):

The mucic acid, $COOH \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot COOH$, first loses the elements of water (2 mols.) giving dehydromucic acid (I.), which is then decomposed into pyromucic acid (II.), carbon dioxide, and water,



Pyromucic acid (m.p. 134°) is very like benzoic acid in properties.

Furfuraldehyde, $C_4H_3O \cdot CHO$ (*furfural*), is obtained quantitatively when pentoses, such as arabinose and xylose (p. 306), are distilled with hydrochloric acid; it may be supposed that the pentose first loses two molecules of water, as indicated,



and then, by a further loss of water, is converted into the aldehyde (III. above).

Furfuraldehyde is usually prepared by heating bran with dilute sulphuric acid and then distilling the product in steam. It boils at 162° , and yields a hydrazone (m.p. 96°), which is practically insoluble in water; by ascertaining the weight of the hydrazone, which can thus be obtained when a vegetable product is distilled with acid, the quantity of the pentoses contained in the sample may be determined.

Furfuraldehyde shows many of the reactions of benzaldehyde. Thus, when shaken with caustic potash, it yields a mixture of furfuralcohol (IV. above) and furancarboxylic acid, just as benzaldehyde gives benzyl alcohol and benzoic acid (p. 440). It may also be successively transformed into *furoin*, $C_4H_3O \cdot CO \cdot CH(OH) \cdot C_4H_3O$,

and *furil*, $C_4H_8O \cdot CO \cdot CO \cdot C_4H_8O$, by reactions exactly analogous to those by which benzaldehyde is converted into benzoin and benzil (p. 441).

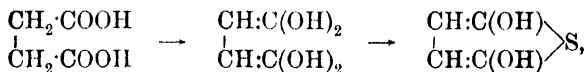
Furfuraldehyde may be very readily detected by the deep-red colour which it gives when aniline is added to its alcoholic solution.

Thiophene, C_4H_4S , was discovered by V. Meyer as a result of the observation that whereas coal-tar benzene shows the indophenin reaction (p. 330), pure benzene (from benzoic acid) does not.

It was at first thought that the blue colouring matter, called indophenin, had been produced by the condensation of one molecule of isatin with one molecule of benzene. V. Meyer showed that indophenin has the composition, $C_{12}H_7ONS$, and that it is produced from isatin and thiophene.

Thiophene may be extracted from coal-tar benzene (which contains about 0.6 per cent. of this sulphur compound) by shaking the crude hydrocarbon with concentrated sulphuric acid; the thiophene dissolves in the form of *thiophenesulphonic acid*, $C_4H_3(SO_3H)S$, which may be isolated by one of the usual methods (p. 417), and converted into its lead salt; when the latter is heated with ammonium chloride, thiophene passes over.

Thiophene may also be obtained by heating sodium succinate with phosphorus trisulphide; it may be assumed that in this reaction the succinic acid is first converted into the dienolic isomeric form, and that the *dihydroxythiophene*, which is first produced,

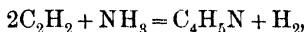


is then reduced by the hydrogen sulphide, which is formed during the reaction. Under similar conditions, lævulic acid (p. 191) is converted into *methylthiophene*, C_4H_3MeS (*thiotolene*), a compound which occurs in crude coal-tar toluene (p. 365).

Thiophene and its derivatives show an extraordinarily close resemblance to benzene and its derivatives; corresponding compounds have almost the same boiling-points, and are very similar in chemical properties. Thiophene boils at 84° .

Pyrrole, C_4H_5N , was discovered in bone-oil by Runge in 1834, and was more fully investigated by Anderson. It is formed by

passing a mixture of acetylene and ammonia through a red-hot tube,



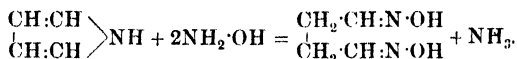
by heating succinimide with zinc-dust (compare thiophene, p. 520), and by heating the ammonium salt of mucic acid with glycerol at about 200° . (Compare formation of pyromucic acid and furan, p. 519.) It boils at 131° , has an odour recalling that of chloroform, and turns brown on exposure to the air.

Pyrrole and its derivatives impart a crimson colouration to a pine-chip moistened with hydrochloric acid and held in the vapour of the substance; in contact with strong acids, pyrrole is rapidly converted into an orange-red substance (pyrrole red), hence the name, pyrrole, from *πυρρός*, red.

Pyrrole is a very feeble base, and also, like diphenylamine (p. 398), shows acidic properties; when heated with potassium it gives a crystalline *potassium* derivative, $\text{C}_4\text{H}_4\text{NK}$, which, however, is hydrolysed by water.

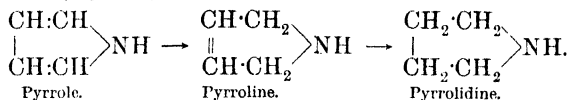
Pyrrole is a compound of very great physiological interest, because the molecules of some of the more important animal and vegetable substances, such as hæmin and chlorophyll contain pyrrole nuclei (p. 577). *Tetraiodopyrrole*, $\text{C}_4\text{I}_4\text{NH}$, is obtained when pyrrole is treated with iodine and an alkali; it forms brown, odourless crystals, which decompose at about 140° , and is sometimes used as an antiseptic in the place of iodoform.

Potassium pyrrole reacts with alkyl halides, giving N-alkyl derivatives, but when these compounds are strongly heated they undergo isomeric change; the alkyl group *migrates* to the adjacent carbon atom and C-alkyl substitution products of pyrrole are formed (compare pyridine methiodide, p. 506). Very interesting reactions also occur when pyrrole is heated with sodium ethoxide and a di- or tri-halogen derivative of methane; with methylene diiodide, for example, pyridine is formed, whereas chloroform and bromoform give 3-*chloro*- and 3-*bromo*-pyridine respectively, a CH or CX group passing into the pyrrole molecule. Another interesting change takes place when pyrrole is treated with hydroxylamine; the closed-chain undergoes *fission* and the dioxime of succindialdehyde is formed,



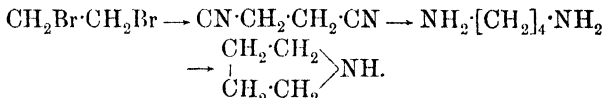
Reduction Products of Pyrrole.—When pyrrole is reduced with zinc and acetic acid, it yields *pyrroline* (b.p. 91°), which on

further reduction with sodium and alcohol is transformed into *pyrrolidine* (b.p. 87°):

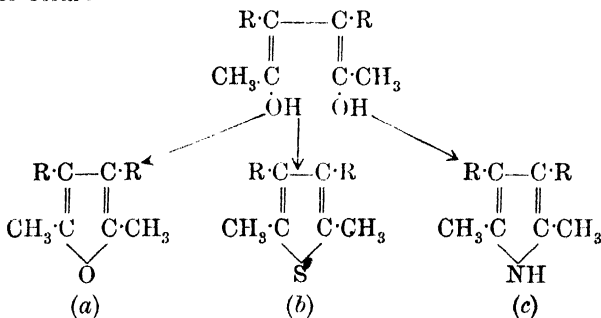


The reduction of pyrrole is accompanied by a great increase in the basic nature of the heterocyclic compound; pyrroline gives stable salts with acids, and pyrrolidine is strongly basic, like diethylamine or piperidine, which it closely resembles in other respects.

Pyrrolidine has been synthesised by reactions exactly similar to those employed in the synthesis of piperidine (p. 509), which may be summarised as follows:



Many derivatives of furan, thiophene, and pyrrole may be prepared synthetically from 1:4- or γ -diketones such as *acetylacetone*, $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$,¹ which contain the grouping, $-\text{CO}\cdot\text{CHR}\cdot\text{CHR}\cdot\text{CO}-$. When such diketo-compounds are treated with (a) sulphuric or hydrochloric acid, (b) phosphorus trisulphide, or (c) ammonia, they are transformed into derivatives of (a) furan, (b) thiophene, and (c) pyrrole respectively. In these changes the diketo-compound probably reacts in the dienolic form:

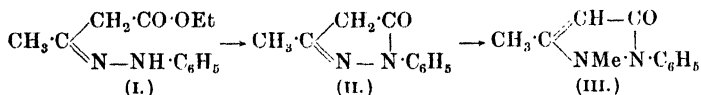


¹ Acetylacetone is obtained when the sodium derivative of ethyl acetoacetate is treated with chloroacetone, $\text{CH}_2\text{Cl}\cdot\text{CO}\cdot\text{CH}_3$, and the product is then submitted to ketonic hydrolysis.

Many compounds of these types have been prepared by similar methods from various 1:4-diketones, which can be obtained synthetically from ethyl acetoacetate.

The Constitutions of Furan, Thiophene, and Pyrrole.—Although the molecules of these three heterocyclic compounds are relatively simple, it is not easy to represent them by satisfactory structural formulæ. In each of those already given (p. 518) there are shown two olefinic bindings, from which it might be inferred that the compound behaved like a di-olefine (p. 94) and combined directly with two molecules of bromine, hydrogen bromide, &c.; this, however, is not the case. With most reagents furan, thiophene, and pyrrole do not give additive products; pyrrole, for example, gives, even with iodine, a tetra-substitution product (p. 521); thiophene reacts readily with chlorine and bromine, giving substitution products, and also forms a *nitrothiophene*, $C_4H_3(NO_2)S$, by direct nitration. In nearly all their reactions, in fact, the three heterocyclic compounds behave like aromatic, rather than aliphatic, substances, and show a benzenoid character, although they are less stable than molecules which contain a benzene nucleus. For these reasons, and in spite of the fact that many syntheses, such as those just given, accord well with the formulæ on p. 518, these structures are unsatisfactory (p. 496). It may be noted that for distinguishing the substitution products, the two carbon atoms next to the O, S, or NH group are lettered, α , the other two, β , in all three formulæ; in the formula for pyrroline (p. 522) it will be seen that the double binding is shown between the two β -carbon atoms, and not between a β - and an α -carbon atom as might have been expected. The reason for this will be given later (Part III.).

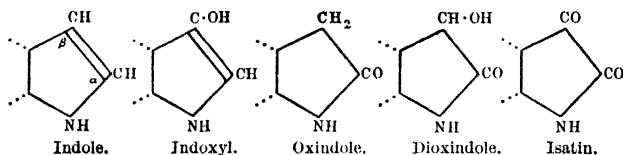
Antipyrine, $C_{11}H_{12}ON_2$ (phenazone), is a 1:2:3-phenyldimethyl-derivative, of a closed-chain compound, $CH \begin{smallmatrix} \diagup NH \cdot NH \\ \diagdown CH \cdot CO \end{smallmatrix}$, which is called *pyrazolone*. It is manufactured by heating ethyl acetoacetate with phenylhydrazine and then methylating the product with methyl chloride under pressure; the hydrazone (I.), which is first formed, loses a molecule of alcohol, giving a 1-phenyl-3-methylpyrazolone (II.) which, when methylated, is converted into a 1:2:3-phenyldimethylpyrazolone (III.). As the structure of this compound (III.) has been determined by other syntheses, it must be concluded that the 1-phenyl-3-methylpyrazolone undergoes isomeric change before it is methylated.



Antipyrine is a crystalline compound (m.p. 113°), and is readily soluble in water; it is a strong mono-acidic base, and is a powerful antipyretic. Its *salicylate* is also used as an antipyretic, under the name of *salipyrine*.

Indole and its Derivatives.

The molecule of indole is composed of a benzene nucleus which is *condensed* (p. 478) in the *o*-position with a pyrrole nucleus and may be called a benzo- or pheno-pyrrole. Indole is related to indigo-blue, and some of its simpler derivatives were prepared by Baeyer in his researches on that very important compound. The following formulæ, based principally on the results of Baeyer's work, show the structures of indole and of some of its derivatives:¹

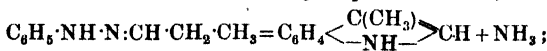


Most of these compounds show tautomerism; indoxyl and oxindole give derivatives of the keto-forms, $-\text{CO}-\text{CH}_2-\text{NH}-$ and $-\text{CH}_2-\text{CO}-\text{NH}-$ respectively, and isatin gives derivatives of the lactim, $-\text{CO}-\text{C}(\text{OH})=\text{N}-$ (p. 516).

Indole, $\text{C}_8\text{H}_7\text{N}$, the parent substance of this group, is related to indene (p. 491), as well as to pyrrole (p. 520), and the other compounds shown above; some of its derivatives, such as tryptophane (p. 552), are of great importance, as they are found among the decomposition products of certain proteins; indole itself occurs in coal-tar, from which it is extracted commercially.

Indole can be obtained by heating oxindole or indigo-white (p. 606) with zinc-dust. It is colourless, melts at 52° , is volatile in steam, and has an odour similar to that of naphthylamine; its vapours and its solutions impart a cherry-red colour to a pine-chip moistened with alcohol and hydrochloric acid (p. 521), and, like indene, it forms a crystalline compound with picric acid. It is only a feeble base, and is converted into resin by acids.

Many indole derivatives have been prepared by heating the phenylhydrazones of aliphatic aldehydes, ketones, and ketonic acids with hydrochloric acid or zinc chloride (Fischer). The hydrazone of prop-aldehyde, for example, gives β -methylindole (*skatole*), a compound which occurs in faeces, and has a very unpleasant smell,

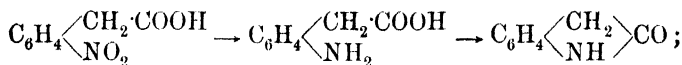


¹ The benzene nucleus is indicated by dotted lines only.

in a similar manner the hydrazone of pyruvic acid (p. 191) gives *indole- α -carboxylic acid*.

Indoxyl, $C_8H_6(OH)N$ (β -hydroxyindole), is produced by fusing phenylglycine-*o*-carboxylic acid with caustic alkalis in the absence of air (p. 608). It forms yellow crystals, melts at 85° , and in alkaline solution undergoes atmospheric oxidation, giving indigo-blue (indigotin).

Oxindole, C_8H_7ON , can be obtained by reducing isatin or dioxindole (see below), and also by the reduction of *o*-nitrophenylacetic acid,



this last reaction shows that oxindole may be regarded as the lactam of *o*-aminophenylacetic acid (p. 516). Oxindole crystallises in colourless needles, melting at 127° , and, in a moist condition, is oxidised to dioxindole on exposure to the air.

Dioxindole, $C_8H_7O_2N$, is obtained by reducing isatin with zinc-dust and hydrochloric acid; it is crystalline, melts at 180° , and when treated with sodium amalgam and water, it is converted into oxindole. In aqueous solution it undergoes atmospheric oxidation to isatin.

Isatin, $C_8H_5O_2N$, is obtained by oxidising indigo-blue with nitric acid; it crystallises in orange-red prisms, melting at 201° , and is practically insoluble in cold water, but it dissolves readily in caustic alkalis, giving *yellow* solutions of salts derived from the *lactim* (p. 524). When isatin is treated with phosphorus pentachloride in benzene solution, it is converted into *isatin chloride*, also a derivative of the lactim, which gives indigotin on reduction with zinc-dust and acetic acid.

Isatin can be synthesised by treating *o*-nitrobenzoyl chloride with silver cyanide, hydrolysing the cyanide to the acid, and then reducing the latter; the *o*-aminobenzoylformic acid, $C_6H_4 \begin{array}{c} \text{CO} \cdot \text{COOH} \\ \text{NH}_2 \end{array}$, thus formed, passes spontaneously into its lactam, isatin.

CHAPTER XXXVI.

VEGETABLE ALKALOIDS.

From very early times many crude products of the vegetable kingdom have been used in medicine, and subsequently the physiologically active compounds, contained in these crude products, were isolated and studied. They were found to be nitrogenous substances, having a basic or alkaline character, and were therefore classed as the *vegetable alkaloids*. This term is still used, but can hardly be defined; it is applied to compounds which differ widely in properties and in constitution, but broadly, a vegetable alkaloid is a nitrogenous, basic compound which has some pronounced physiological action. The term, alkaloid, may also be applied to similar active substances, obtained from the animal kingdom, or even prepared synthetically, and not known to occur in nature. The following general statements refer more particularly to the important medicinal products of the vegetable kingdom.

Most alkaloids are composed of carbon, hydrogen, oxygen, and nitrogen, have a high molecular weight, and are crystalline and non-volatile, but a few, notably *coniine* and *nicotine*, are composed of carbon, hydrogen, and nitrogen only, and are volatile liquids; with the exception of these liquid compounds, which are readily soluble, the alkaloids are usually sparingly soluble in water, but they dissolve in alcohol, chloroform, ether, and other organic solvents; with acids, they form salts, which are usually soluble in water and crystallise well. Most alkaloids are optically active, usually levorotatory (*coniine* is dextrorotatory), and have been largely used for the resolution of externally compensated acids. Many alkaloids have a very bitter taste, and are excessively poisonous; many, moreover, are extensively used in medicine, and their value in this respect can hardly be overrated.

The extraction of alkaloids from plants, and their subsequent purification, are frequently matters of considerable difficulty, partly

because, in many cases, two or more alkaloids occur together, partly because soluble, neutral, and acidic substances, such as glucosides, tannic acid, malic acid, &c., are often also present in large quantities. Generally speaking, the alkaloids may be extracted by treating the macerated vegetable matter with dilute acids, which convert the alkaloids into soluble salts. The filtered solution may then be treated with sodium carbonate or ammonia to liberate the alkaloids, which, being sparingly soluble, are usually precipitated, and may be separated by filtration; if not, the alkaline solution is extracted with ether, chloroform, &c.¹ An alternative procedure is to macerate the vegetable product with alkali, extract the alkaloid with a solvent, and then shake the solution with a dilute acid; the neutral substances remain in the organic solvent, while the alkaloid dissolves in the form of a salt. The alkaloid or its salt is then further purified by recrystallisation, or in some other manner. Several examples of the extraction of alkaloids are given later in more detail (pp. 538, 539, 541).

Most alkaloids give insoluble precipitates with a solution of tannic, picric, phosphomolybdic, or phosphotungstic acid, and with a solution of mercuric iodide in potassium iodide, &c.; these reagents, therefore, are often used for their detection and isolation. In cases of alkaloid poisoning, it is usual, after the stomach-pump has been used, to wash out the stomach with dilute tannic acid, or to administer strong tea (which contains tannin), in order to render the alkaloids insoluble, and relatively harmless.

Generally speaking, the alkaloids are tertiary aromatic bases, but the constitutions of many of them have not yet been fully established, owing partly to their complexity, partly to the difficulty of resolving them into simpler compounds, which throw any light on their structures. The more important general methods, which have been used to determine the constitution of an alkaloid, may be summarised under the following headings:

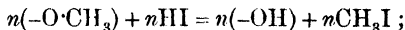
(1) Hydrolysis; for the decomposition of esters (p. 534) and amides (p. 533).

(2) Fusion with alkali, heating with zinc-dust, &c.; under such

¹ A mixture of benzene (3 vols.) and amyl alcohol (1 vol.) is often used by pharmacists, under the name of 'benzolated amyl alcohol,' as a solvent for alkaloids.

treatment many alkaloids are resolved into simpler compounds, such as pyridine, quinoline, isoquinoline, &c.

(3) Decomposition with hydriodic acid. Many alkaloids contain one or two, sometimes three or more, methoxy-groups, ($-\text{O}\cdot\text{CH}_3$), united with a benzenoid nucleus, and when they are heated with concentrated hydriodic acid, they give methyl iodide and a hydroxy-compound (compare anisole, p. 426),



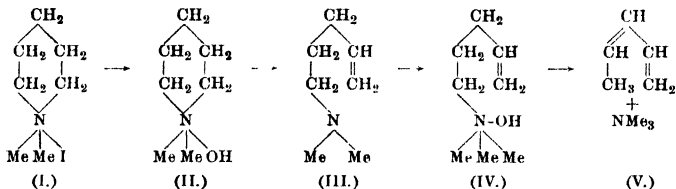
by estimating the methyl iodide, obtained from a given quantity of a compound of known molecular weight, it is possible to ascertain the number of methoxy-groups in the molecule; other alkyloxy-groups may be determined in a similar manner. This method was first devised by Zeisel, and is of general application; it is conveniently carried out as follows:

A weighed quantity (0.2–0.4 g.) of the alkaloid is placed in a long-necked distillation flask, together with excess (15–25 c.c.) of *distilled* hydriodic acid (b.p. 126°), free from hydrogen sulphide.¹ The outlet tube of the flask is connected with two small wash-bottles (in series), which contain a concentrated aqueous-alcoholic solution of silver nitrate, and a slow stream of carbon dioxide (free from hydrogen chloride) is passed into the hydriodic acid and through the whole apparatus. The distillation flask is heated in an oil- or glycerol-bath, so that the hydriodic acid is just raised to its boiling-point. The methyl iodide, which is formed, reacts with the silver nitrate, and the precipitated silver iodide is afterwards estimated in the usual way.

(4) Exhaustive methylation followed by decomposition of the product. This is a process which is used for eliminating a nitrogen atom from a base, and the first step is to convert the base into a quaternary hydroxide by treatment with methyl iodide and silver (hydr)oxide alternately. Piperidine, for example, is thus transformed into N-methylpiperidine hydriodide, N-methylpiperidine, *dimethylpiperidonium iodide* (i.) and *dimethylpiperidonium hydroxide* (ii.). When strongly heated, this hydroxide loses the elements of water and gives *pentylenedimethylamine* (iii.). (Compare tetraethylammonium hydroxide, p. 197.) This base is now methylated and the quaternary hydroxide (iv.) is finally de-

¹ Hydriodic acid, prepared from iodine with the aid of hydrogen sulphide, often contains the latter; in that case the precipitated silver iodide is contaminated with silver sulphide, and should be boiled with dilute nitric acid before it is collected.

composed into 1-methylbutadiene (*piperylene*) (v.) and trimethylamine. It may be assumed that the primary product of this last change is $\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CH}\cdot\text{CH}_2$, which then undergoes isomeric change into 1-methylbutadiene:



(5) Graded oxidation; with the aid of various oxidising agents, the molecule of the alkaloid may be disintegrated, giving simpler compounds, the structures of which may be determined (compare p. 538).

By the combination of methods such as those indicated above, the structures of many of the less complex alkaloids have been settled and the compounds themselves have then been synthesised. Even when the complete constitutional formula is still undetermined, it may have been possible to prove that a given alkaloid is derived from some known compound. A classification of the alkaloids based on a knowledge of their structures thus becomes possible, and is adopted in the following account of the more important members of this group.

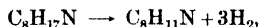
Alkaloids derived from Pyridine.

Coniine, $\text{C}_8\text{H}_{17}\text{N}$, one of the relatively simple alkaloids, is contained, with other bases, in the spotted hemlock (*Conium maculatum*), more particularly in the seeds, from which it may be obtained by distillation with caustic soda. It is a colourless oil, boiling at 166° , and is readily soluble in water; it has a most penetrating odour, and turns brown on exposure to the air. Coniine is a strong secondary base; its *hydrochloride*, $\text{C}_8\text{H}_{17}\text{N}\cdot\text{HCl}$, and most of its other salts are readily soluble in water. Both the base and its salts are exceedingly poisonous,¹ and cause death

¹ Persons condemned to death in ancient Greece were often poisoned with hemlock; it was in this way that the life of Socrates was ended.

in a short time by paralysing the muscles of respiration. Coniine is dextrorotatory.

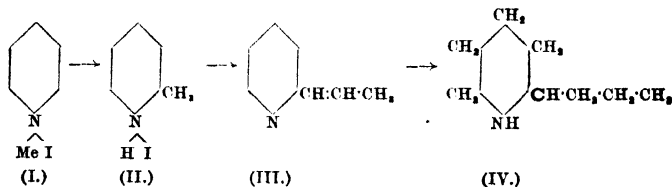
Coniine hydrochloride distilled over heated zinc-dust, gives *conyryne*,¹



which on oxidation yields pyridine- α -carboxylic acid (picolinic acid, p. 511). Conyryne, therefore, is either β -propyl- or α -isopropyl-pyridine. Hydriodic acid converts coniine into *normal* octane and ammonia; the side-chain in conyryne, therefore, is a *normal* propyl- and not an iso-propyl-group. From these and other facts it would appear that coniine is *D*- α -propylpiperidine (iv.). This structure was fully confirmed by Ladenburg's synthesis of the compound; as this was the first case in which a naturally occurring alkaloid was obtained artificially, the synthesis, described below, is of great historical interest.

Coniine was synthesised by Ladenburg in the following manner:

Piperidine (which can be obtained from its elements, p. 509) is converted into pyridine² (p. 505), and from the latter the methiodide (i.) is prepared. This salt is heated at 300°, whereby it is transformed into α -picoline (methylpyridine) hydriodide (ii.) (compare p. 506). The α -picoline is heated with acetaldehyde (or paraldehyde) at 250°, and transformed into 2-propenylpyridine (iii.), which is then reduced to 2-propylpiperidine (*dl*-coniine) (iv.) with sodium and alcohol. The *dl*-coniine is next converted into its *d*-tartrate, and the salt is fractionally crystallised (p. 278); the more sparingly soluble salt of the *d*-base, which crystallises from the solution (leaving the salt of the *l*-base in the mother-liquor), is separated and decomposed with alkali. The *d*-coniine thus obtained is identical with that from hemlock.



Nicotine, $\text{C}_{10}\text{H}_{14}\text{N}_2$, is present in the leaves of the tobacco-plant (*Nicotiana tabacum*), combined with malic or citric acid; it may be obtained from tobacco-leaves by the methods already indicated (p. 527).

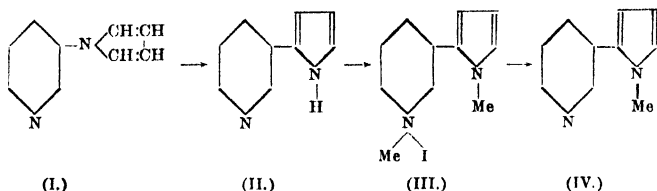
¹ As a rule, strongly heated zinc-dust acts as a reducing agent (p. 362).

² Although coniine is a derivative of piperidine, it is necessary first to convert the piperidine into pyridine in order to substitute a methyl group for an α -hydrogen atom of the nucleus (p. 506).

It is a colourless oil, which boils at 247° , has a very pungent odour, and rapidly turns brown on exposure to the air; it is readily soluble in water and organic solvents, and is lævorotatory. Nicotine is exceedingly poisonous, two or three drops taken into the stomach being sufficient to cause death in a few minutes. It shows no very characteristic reactions, but its presence may be detected by its extremely pungent odour (which recalls that of a foul tobacco-pipe).

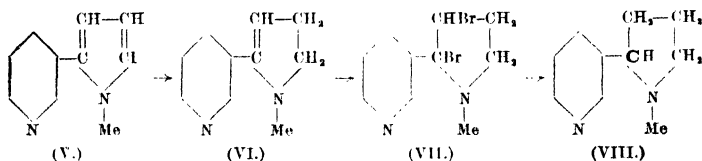
Nicotine is a di-acidic base, and forms crystalline salts, such as the *hydrochloride*, $C_{10}H_{14}N_2 \cdot 2HCl$. It combines directly with two molecules of methyl iodide, yielding *nicotine dimethiodide*, $C_{10}H_{14}N_2 \cdot 2CH_3I$, a fact which shows that it is a di-tertiary base (p. 518). When oxidised with chromic acid it yields nicotinic acid (pyridine- β -carboxylic acid, p. 511); it is, therefore, a β -pyridine derivative.

The results of various investigations having indicated that the β -substituent was a univalent radical derived from N-methylpyrrolidine (p. 522), the synthesis of nicotine was accomplished by Pictet as follows:¹ Nicotinic acid (pyridine- β -carboxylic acid) was transformed successively into its ester and its amide, and the latter was converted into β -aminopyridine by Hofmann's reaction (p. 193). The salt of β -aminopyridine and mucic acid (p. 288), when distilled, yielded N- β -pyridylpyrrole (I.), which, like other N-substitution products of pyrrole (p. 521), underwent isomeric change into β -pyridyl- α -pyrrole (II.) when it was passed through a heated tube. This C-pyrrole derivative, with potash and methyl iodide, gave the product (III.), which, distilled with lime, was converted into *nicotyrine* (IV.) (a base which is obtained by the oxidation of nicotine with silver oxide).

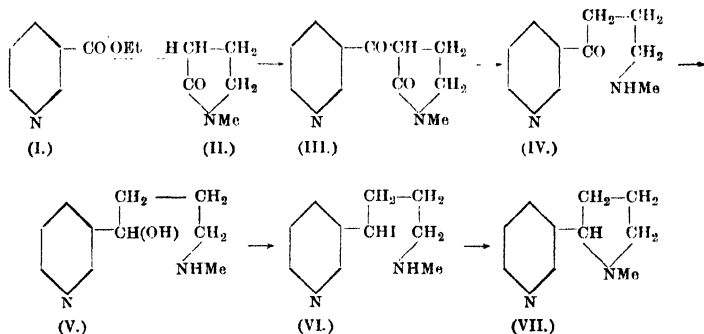


¹ The syntheses of nicotine and those of some of the simpler alkaloids described in this chapter will indicate the manner in which it is possible to build up relatively complex molecules, when their structures have been determined by analytical processes, such as those already mentioned (p. 527); their committal to memory is unnecessary except for students working for an Honours Degree examination.

Now nicotyrine could not be directly reduced to nicotine, because those reagents which effected the reduction of the pyrrole ring also added hydrogen to the pyridine nucleus. This difficulty was overcome by treating the nicotyrine with iodine and caustic soda, and reducing the iodo-substitution product (V.) with zinc and hydrochloric acid. The *dihydronicotyrine* (VI.), thus formed, was converted into its dibromide (VII.), which, on reduction with tin and hydrochloric acid, yielded *dl*-nicotine (VIII.); the resolution of this base with tartaric acid furnished *l*-nicotine, identical with the naturally occurring compound :

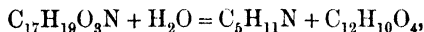


More recently a somewhat simpler synthesis has been devised by Späth and Bretschneider : The ethyl ester of nicotinic acid (I.) condenses with *N*-methyl- α -pyrrolidone (II.), in the presence of sodium ethoxide, yielding a substance (III.) which changes into (IV.), on being heated with hydrochloric acid (with the loss of carbon dioxide). This ketone (IV.) is then reduced (zinc-dust and alkali) to the corresponding alcohol (V.), which is converted into the iodide (VI.) with hydriodic acid. Aqueous alkali transforms the iodide into *dl*-nicotine (VII.), which may be resolved as before :



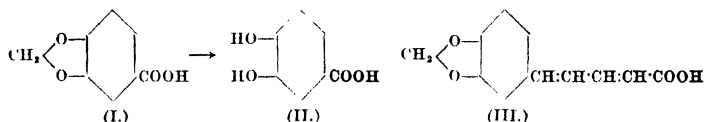
Piperine, $\text{C}_{17}\text{H}_{19}\text{O}_3\text{N}$, occurs to the extent of about 8–9 per cent. in pepper, especially in black pepper (*Piper nigrum*), from which it is easily obtained by warming the powdered pepper with milk of lime, evaporating to dryness, and extracting the residue with ether.

It melts at 128° , and is almost insoluble in water; it is only a very weak base, is optically inactive, and is not of any physiological importance. On hydrolysis it gives piperidine (p. 509) and piperic acid,

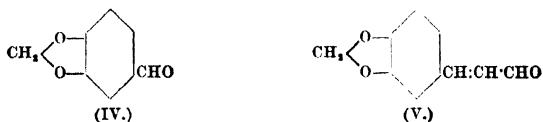


and it may be obtained again by treating piperidine with the chloride of piperic acid.

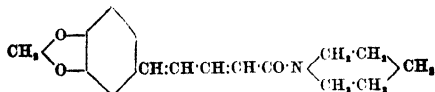
Piperic acid unites directly with four atoms of bromine, yielding a compound, $C_{12}H_{10}O_4Br_4$, and therefore its molecule probably contains two ethylenic linkages. On oxidation it gives piperonylic acid, which is known to have the structure (I.), because it is decomposed by boiling hydrochloric acid into protocatechuic acid (II.) and carbon. Piperic acid therefore must contain only one (unsaturated) side-chain (which gives rise to the carboxyl-group of piperonylic acid), and is represented by (III.).



The structure of piperic acid having been determined, the complete synthesis of piperine was accomplished in the following manner: Protocatechuic aldehyde, obtained from catechol by the Tiemann-Reimer reaction, is treated with methylene diiodide and alkali and is thus transformed into *piperonal* (IV.), a compound obtained by oxidising piperic acid with permanganate. Piperonal is condensed with acetaldehyde to yield the compound (V.), which, with sodium acetate and acetic anhydride



(Perkin reaction), gives piperic acid (see above). The chloride of piperic acid reacts with piperidine to form piperine, and thus the structure of the alkaloid is proved to be as shown below:



Atropine, $C_{17}H_{23}O_3N$ (daturine), is prepared from the deadly nightshade (*Atropa Belladonna*) which, like henbane (*Hyoscyamus niger*), and *Datura Stramonium*, contains various isomeric and closely related alkaloids, of which atropine and *hyoscyamine* are

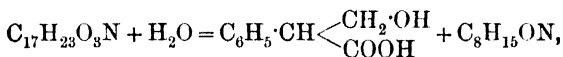
the more important; the latter is optically active, but readily racemises on treatment with bases, giving atropine. Atropine, therefore, is *dl*-hyoscyamine.

Atropine crystallises in prisms, and melts at 118° ; it is readily soluble in alcohol and ether, but almost insoluble in water.

It is a strong base, and forms well-characterised salts, of which the *sulphate*, $(C_{17}H_{23}O_3N)_2 \cdot H_2SO_4$, is readily soluble, and, therefore, most commonly used in medicine; both the base and its salts are extremely poisonous, about 0.15–0.2 g. causing death. Atropine sulphate is largely used in ophthalmic surgery, owing to its remarkable property of dilating the pupil, when its solution is placed on the eye.

Test for Atropine.—When a trace of atropine is moistened with fuming nitric acid, and evaporated to dryness on a water-bath, it yields a yellow residue, which, on the addition of alcoholic potash, gives an intense violet solution, the colour gradually changing to red.

When atropine is boiled with baryta-water it is readily hydrolysed, yielding *dl*-tropic acid and tropine,

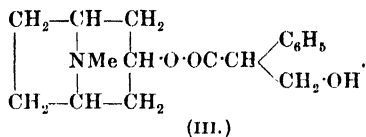
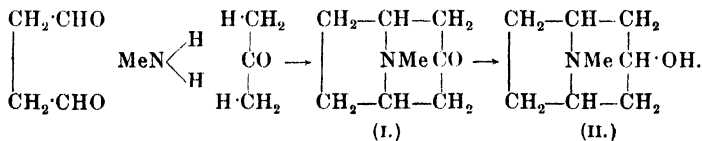


and conversely, tropic acid and tropine react in the presence of hydrochloric acid to form atropine.

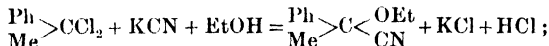
Tropine, thus proved to be an alcohol, is oxidised by chromic acid to a ketone, *tropinone*, $C_8H_{13}ON$; it loses the elements of water when it is heated with acids, giving *tropidine*, $C_8H_{13}N$, an unsaturated base. Tropidine, by the processes of exhaustive methylation and decomposition of the resulting quaternary hydroxide (compare piperidine, p. 528) is converted into a di-olefinic tertiary base, $C_7H_9 \cdot NMe_2$, which, by a repetition of the same processes, is finally decomposed into *cycloheptatriene*, $CH_2 < \begin{matrix} CH:CH \cdot CH \\ CH:CH \cdot CH \end{matrix}$, trimethylamine and water. The molecule of tropine, therefore, contains a closed-chain of seven carbon atoms, a conclusion which is confirmed by the fact that (normal) pimelic acid (p. 261) can also be obtained from tropine by a series of reactions, which also involves exhaustive methylation, &c. Tropine, degraded by other methods, gives α -ethylpyridine.

These facts indicated that the molecule of tropine contained, not only a saturated closed-chain of seven carbon atoms, but also a saturated closed-chain consisting of five atoms of carbon and one atom of nitrogen. After a great deal of further investigation its probable structure (II.) was determined, and finally established by a long and difficult synthesis

by Willstätter. A very simple synthesis was accomplished later by Robinson, who obtained tropinone (I.) by the interaction of succinaldehyde (p. 521), methylamine, and acetone¹; the tropinone can be reduced to tropine (II.), and finally this alcohol can be converted into its tropic ester, which is atropine (III.).



Tropic acid has been synthesised as follows: Acetophenone is converted into the dichloride with phosphorus pentachloride, and the product is treated with alcoholic potassium cyanide,



this nitrile, heated with hydrochloric acid, undergoes hydrolysis and also loses the elements of alcohol, yielding atropic acid, $\text{PhC}(\text{CH}_2) \cdot \text{COOH}$. By the successive action of hydrogen chloride and aqueous alkali the elements of water are added to this unsaturated acid and *dl*-tropic acid (p. 534) is formed.

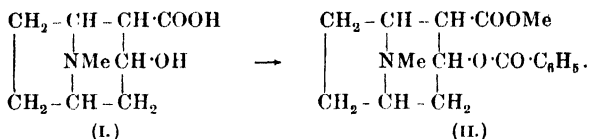
Cocaine, $\text{C}_{17}\text{H}_{21}\text{O}_4\text{N}$, and several other alkaloids of less importance, are contained in coca-leaves (*Erythroxylon Coca*), in combination with cinnamic and other acids.

It crystallises in colourless prisms, melts at 98° , is lævorotatory, and is sparingly soluble in water; it forms well-characterised salts, of which the *hydrochloride*, $\text{C}_{17}\text{H}_{21}\text{O}_4\text{N} \cdot \text{HCl}$ is generally employed in medicine. Cocaine is a very valuable local anæsthetic, and is used in minor surgical operations, as its external application takes away all sensation of pain; it is poisonous, however, one grain injected subcutaneously having been attended with fatal results.

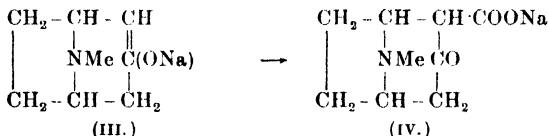
When heated with acids or alkalis, cocaine is readily hydrolysed, with formation of benzoic acid, methyl alcohol, and *lecgonine*, which is a

¹ Calcium acetonedicarboxylate gave a better yield than acetone; the *calcium tropinonedicarboxylate* thus obtained was converted into the acid and the latter was decomposed by heat.

monocarboxylic acid derived from tropine (see p. 535), and has the constitution (I.),



Cocaine (II.) is the methyl ester of benzoyl-*l*-ecgonine, and is formed when the methyl ester of *l*-ecgonine is benzoylated. *dl*-Ecgonine has been synthesised from tropinone (see p. 535). This ketone gives a sodium derivative (III.) which, on treatment with carbon dioxide, yields the sodium salt of tropinonecarboxylic acid (IV.):

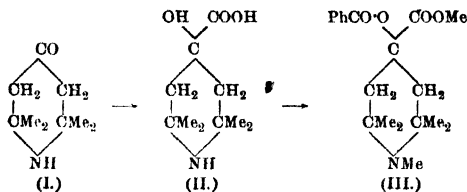


On reduction with sodium amalgam this tropinone derivative is converted into *dl*-ecgonine, which closely resembles the *l*-isomeride obtained from cocaine in most respects.

Synthetic Alkaloids.

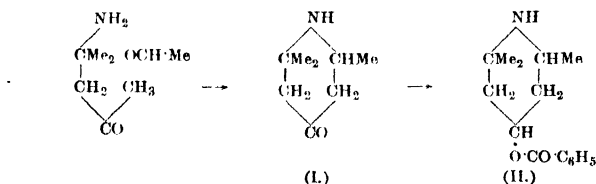
Since the grouping $\text{>N}-\overset{\overset{|}{|}}{\underset{\underset{|}{|}}{\text{C}}}-\text{C}-\text{CO}-\text{O}-\text{R}$, which occurs in its molecule, might be responsible for the anæsthetic properties of cocaine, several other substances containing this or a similar group have been prepared synthetically, and have, in fact, been found to be useful as anæsthetics.

α -Eucaine is prepared by the following series of reactions: Triacetoneamine (I.), which is obtained by condensing acetone with ammonia, is treated with hydrogen cyanide, and the cyanohydrin thus formed is hydrolysed; the product (II.) is then successively benzoylated and methylated, and yields α -eucaine (III.),



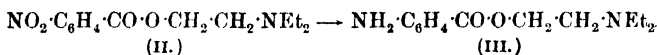
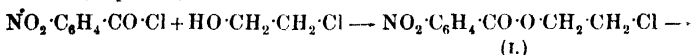
α -Eucaine is less toxic than cocaine but has the disadvantage of being somewhat irritant when injected, and has now been superseded by β -eucaine, novocaine, and stovaine.

β -Eucaine is prepared from *diacetoneamine*, $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CMe}_2\cdot\text{NH}_2$, a simpler condensation product of acetone and ammonia. The hydrogen oxalate of this base, when it is heated with paraldehyde (or acetal) in alcoholic solution, yields the oxalate of *vinyl diacetoneamine*, which is a trimethylketopiperidine (I.) On reduction with sodium and boiling amyl alcohol, this keto-derivative gives the corresponding secondary alcohol (of which there are two *dl*-stereoisomeric forms, melting at 163° and 138° respectively). The base melting at 138° gives a hydrochloride which, heated with benzoyl chloride, yields the hydrochloride of β -eucaine (II.) :



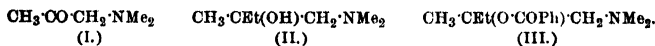
β -Eucaine has anaesthetic properties equal to those of cocaine, and its salts are easily soluble in water and are stable in boiling solution; they can therefore be readily sterilised. β -Eucaine is also known as *benzamine*.

Novocaine is quite a different type of compound and may be prepared as follows: Ethylene chlorohydrin is first condensed with *p*-nitrobenzoyl chloride and the product (I.) is treated with diethylamine. The compound so formed (II.) is then reduced to the base (III.), the hydrochloride of which (m.p. 156°) is novocaine:



Novocaine, also called *procaine*, is a powerful local anaesthetic, less toxic than cocaine; it is much used in dentistry and minor surgical operations.

Stovaine is also a well-known local anaesthetic. It may be prepared by treating chloroacetone with dimethylamine, converting the product (I.) into a tertiary alcohol (II.) with magnesium ethyl bromide, and then benzoylating the alcohol: stovaine is the hydrochloride of the base (III.),



Alkaloids derived from Quinoline.

Quinine, $\text{C}_{20}\text{H}_{24}\text{O}_2\text{N}_2$, cinchonine (see p. 539), and about thirty other allied alkaloids, occur in the bark of various species of

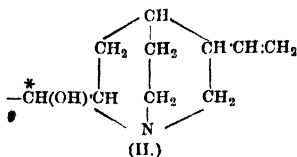
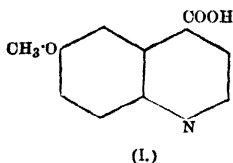
Cinchona and related plants; the alkaloids are present in the bark, combined with cincho-tannic and quinic acids,¹ and some barks contain as much as 10 per cent. of quinine.

The powdered bark is extracted with dilute sulphuric acid, and the solution of the sulphates is treated with caustic soda. The crude mixture of precipitated alkaloids is dissolved in alcohol, the solution is neutralised with sulphuric acid, and the sulphates, which are deposited, are repeatedly recrystallised from water. Quinine sulphate is the least soluble, and separates out first, the sulphates of cinchonine and of the other alkaloids remaining in solution; from the purified sulphate, quinine may be obtained by precipitation with ammonium hydroxide.

Quinine crystallises with water (3 mols., one of which is lost at about 20°), melts at about 173° when anhydrous, and is only very sparingly soluble (1 in 1906 at 15°) in water; it is a very feeble di-acidic base, and generally forms well-defined salts, such as the *sulphate*, $(C_{20}H_{24}O_2N_2)_2 \cdot H_2SO_4 \cdot 8H_2O$. Many of its salts are soluble in water, and are very much used in medicine as tonics, and in cases of malaria and other intermittent fevers; as these salts have an intensely bitter taste, various simple derivatives of quinine, having little or no taste, have been prepared for use in medicine. Quinine is lævorotatory.

Test for Quinine.—When a solution of a salt of quinine is treated with a slight excess of chlorine- or bromine-water, and ammonium hydroxide is then added, a highly characteristic, emerald-green colouration is produced; quinine is also characterised by the fact that *dilute* solutions of its salts show a beautiful light-blue fluorescence.

Quinine is a di-tertiary base, because it combines with methyl iodide to form *quinine dimethiodide*, $C_{20}H_{24}O_2N_2 \cdot (CH_3I)_2$; it is a derivative of quinoline, because on oxidation with chromic acid it yields *quininic acid* or *6-methoxyquinoline-4-carboxylic acid* (I.):



¹ *Quinic acid*, $C_6H_7(OH)_4 \cdot COOH$, crystallises in prisms, and melts at 162°. It is a tetrahydroxyhexahydrobenzoic acid, and is optically active.

The carbon atom which remains in the form of the carboxyl-group in this acid is probably that marked with an asterisk in a complex of the structure (II.).

Cinchonine, $C_{19}H_{22}ON_2$, accompanies quinine in almost all the cinchona-barks, and is present in some kinds (in the grey bark, from Huanuco in Peru) to the extent of 2 per cent.

In order to prepare cinchonine, the mother-liquors from the crystals of quinine sulphate (see p. 538) are treated with caustic soda, and the precipitate is dissolved in the smallest possible quantity of boiling alcohol; the crude cinchonine, which separates from the cold solution, is then converted into the sulphate, and this salt is crystallised from water.

Cinchonine crystallises in prisms, decomposes at about 240° , and resembles quinine in ordinary properties, but is dextrorotatory; its salts are antipyretics, but are much less active than those of quinine.

Oxidising agents, such as nitric acid or potassium permanganate, readily attack cinchonine, and convert it into various substances, one of the more important of which is *cinchoninic acid* (*quinoline-4-carboxylic acid*).

The formation of this acid and other facts prove that cinchonine is a quinoline-derivative; its structure is very closely related to that of quinine; quinine, in fact, is a *methoxycinchonine*.

Strychnine, $C_{21}H_{22}O_2N_2$, and brucine, two highly poisonous alkaloids, are present in the seeds of *Strychnos Nux-vomica* and of *Strychnos Ignatii* (Ignatius' beans), which contain 2–3 per cent. of the mixed bases.

Powdered nux-vomica is boiled with dilute alcohol, and the filtered solution is evaporated and treated with lead acetate to precipitate tannin, &c. The filtrate is then freed from lead with hydrogen sulphide, and the filtered solution is mixed with magnesia. The precipitated alkaloids are separated, and warmed with a little alcohol, which dissolves the brucine; the residual *strychnine* is purified by recrystallisation from alcohol.

The alcoholic solution of the brucine—which still contains strychnine—is evaporated, and the residue dissolved in dilute acetic acid; this solution is now evaporated to dryness on a water-bath, during which process the strychnine acetate decomposes, with loss of acetic acid and separation of the free base. The stable brucine acetate is dissolved in water, the filtered solution is treated with caustic soda, and the precipitated *brucine* is purified by recrystallisation from aqueous alcohol.

Strychnine crystallises in rhombic prisms, and decomposes at about 245° ; although it is very sparingly soluble in water (1 part in 6400 at 25°), its solution has an intensely bitter taste, and is very poisonous. Strychnine, in fact, is one of the more poisonous alkaloids, half a grain of the sulphate having caused death in twenty minutes.

Test for Strychnine.—Strychnine is very readily detected, as it shows many characteristic reactions, of which the following is the most important: When a small quantity of powdered strychnine is treated with a little concentrated sulphuric acid in a porcelain basin, and a little powdered potassium dichromate is then dusted over the liquid, an intense violet solution, which gradually becomes bright red, and then yellow, is produced.

Although the molecule of strychnine contains two atoms of nitrogen, it is, like brucine, only a mono-acidic base, forming salts, such as the *hydrochloride*, $C_{21}H_{22}O_2N_2 \cdot HCl$; many of the salts are soluble in water. It is a (lævorotatory) tertiary base, and combines with methyl iodide to form *strychnine methiodide*, $C_{21}H_{22}O_2N_2 \cdot CH_3I$, a quaternary salt.

When strongly heated with potash, strychnine yields, among other products, *quinoline*; probably, therefore, it is a derivative of this base.

Brucine, $C_{23}H_{26}O_4N_2$, crystallises in prisms, with $4H_2O$, and melts, when anhydrous, at 178° . It is more readily soluble in water and in alcohol than strychnine, and, although very poisonous, it is not nearly so deadly as the latter (its physiological effect is only about $\frac{1}{24}$ th of that of strychnine).

Test for Brucine.—When a solution of a brucine salt is treated with nitric acid, a deep brownish-red colouration is obtained, and the solution becomes yellow when it is warmed; if now stannous chloride is added, an intense violet colouration is produced. This colour reaction serves as a delicate test, both for brucine and for nitric acid, as it may be carried out with very small quantities of either compound.

Although its molecule contains two atoms of nitrogen, brucine, like strychnine, is a mono-acidic (lævorotatory) base. The *hydrochloride*, for example, has the composition, $C_{23}H_{26}O_4N_2 \cdot HCl$; brucine is also a tertiary base, and combines with methyl iodide to form *brucine methiodide*, $C_{23}H_{26}O_4N_2 \cdot CH_3I$.

Alkaloids contained in Opium.

The juice of certain kinds of poppy-heads (*Papaver somniferum*) contains a great variety of alkaloids, of which *morphine* is the most important, but *codeine*, *narcotine*, *thebaine*, and *papaverine* may also be mentioned. All these compounds are present in the juice in combination with *meconic acid*,¹ and partly also with sulphuric acid. When incisions are made in the poppy-heads, and the juice which exudes is left to dry, it assumes a pasty consistency, and is called *opium*. An alcoholic tincture of opium, containing 1 g. of anhydrous morphine per 100 c.c., is known as *laudanum*.

Preparation of Morphine.—Opium is extracted with hot water, and the extract is boiled with milk of lime, and filtered from the precipitate, which contains the meconic acid, and all the alkaloids, except morphine. The filtrate is then concentrated, digested with ammonium chloride until ammonia ceases to be evolved (to decompose the soluble calcium derivative of morphine), and kept for some days; the morphine, which separates, is collected and purified by recrystallisation from boiling alcohol.

Morphine, $C_{17}H_{19}O_3N$, crystallises in colourless prisms, with $1H_2O$, and is only sparingly soluble in water and cold alcohol, but dissolves in caustic alkalis and in lime-water, from which it is reprecipitated on the addition of acids; it has, in fact, the properties of a phenol. At the same time, it is a mono-acidic (laevorotatory) base, and forms well-characterised salts with acids; the *hydrochloride*, $C_{17}H_{19}O_3N \cdot HCl \cdot 3H_2O$, crystallises from water in needles, and is the salt commonly employed in medicine. Morphine is a tertiary base, and gives with methyl iodide *morphine methiodide*, $C_{17}H_{19}O_3N \cdot CH_3I$.

Morphine has a bitter taste, and is so poisonous that one grain of the hydrochloride may be a fatal dose; the system, however, may become so accustomed to the habitual use of opium that, after a time, very large quantities may be taken daily without fatal effects. Morphine is extensively used in medicine as a soporific, especially in cases of intense pain.

Tests for Morphine.—When a little iodic acid is dissolved in

¹ *Meconic acid*, $C_8H_6O_2(OH)(COOH)_2$, is an aliphatic closed-chain hydroxy-dicarboxylic acid. It gives, with ferric chloride, an intense dark-red colouration. In cases of suspected opium-poisoning this acid is always tested for, owing to the ease with which it can be detected by this colour reaction.

water, and a few drops of a solution of morphine hydrochloride are added, a brownish colouration is at once produced, owing to the liberation of iodine, and the solution then gives, with starch-paste, a deep-blue colouration.

A solution of morphine, or of a morphine salt, gives a deep-blue colouration with ferric chloride, but perhaps the most delicate test for the alkaloid is the following: A trace of morphine is dissolved in concentrated sulphuric acid, and the solution is kept during fifteen hours; if then treated with nitric acid, it gives a bluish-violet colour, which changes to blood-red. This reaction is very delicate, and is well shown by 0.01 milligram of morphine.

The molecule of morphine contains two hydroxyl-groups, one of which is phenolic, the other alcoholic; it is to the presence of the phenolic hydroxyl-group that morphine owes its property of dissolving in alkalis and giving a blue colour with ferric chloride. *Heroin* is the diacetyl-derivative of morphine.

When heated with potash and methyl iodide, morphine gives *methyl-morphine*, $C_{17}H_{17}ON(OCH_3) \cdot OH$, a substance which is identical with *codeine* (p. 541). Codeine is insoluble in alkalis, and, therefore, is not a phenol; it behaves, however, like an alcohol, and gives, with acetic anhydride, *acetylcodeine*, $C_{17}H_{17}ON(OCH_3) \cdot OAc$.

When morphine is distilled with zinc-dust a considerable quantity of phenanthrene is obtained, together with basic substances; it is thus proved that the molecule of morphine (and also that of codeine) contains a phenanthrene complex.

Apomorphine, $C_{17}H_{17}O_2N$, is formed, together with water, when morphine hydrochloride is heated with concentrated hydrochloric acid at $140-150^\circ$; its hydrochloride is used in medicine as an emetic.

CHAPTER XXXVII.

AMINO-ACIDS AND RELATED COMPOUNDS.

¹ **The amino-acids**, of which glycine (p. 202) is an example, are substances of very great physiological importance. Many of them are obtained by the hydrolysis with acids, alkalis, or

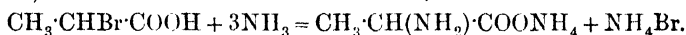
¹ The subject-matter of this and the two following chapters deals more particularly with substances of importance to students of medicine, and to others who are not merely studying for a *pass* degree examination.

digestive enzymes of those highly complex components of animals and plants, which are termed the **proteins** (p. 572); therefore it is concluded that the complex molecule of a protein is produced in organisms by the condensation of a large number of molecules of relatively simple amino-acids.

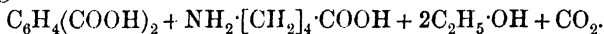
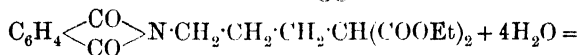
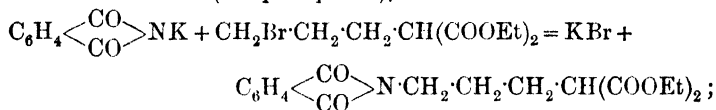
As a rule the product of hydrolysis of a protein is a mixture of some 14–19 different amino-acids, and the separation of its various components is a task of great difficulty. This difficulty is due partly to the complexity of the mixture, but more particularly to the fact that these amino-acids are generally very readily soluble in water, but are insoluble in ether and in all other solvents, which do not mix with water, except the higher alcohols; consequently they cannot be easily extracted from their aqueous solutions; further, they cannot be distilled, and, when impure, they do not crystallise readily. Owing mainly to the work of E. Fischer, who devised new synthetical methods of preparation, and new processes for the separation and isolation of amino-acids from the products of protein-hydrolysis, these difficulties have been largely overcome.

The more important general synthetical methods of preparation are the following:

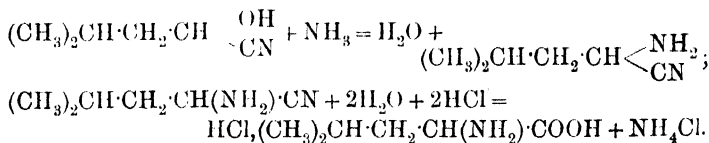
(1) The halogen substitution products of aliphatic acids (pp. 165, 166) are treated with alcoholic ammonia,



(2) The esters of halogen acids are treated with potassium phthalimide, and the products are hydrolysed with hydrochloric acid at about 200° (compare p. 459),



(3) The cyanohydrin of an aldehyde or ketone is treated with the theoretical quantity of ammonia—or an aldehyde or ketone is treated with ammonium sulphate and potassium cyanide—and the nitrile of the α -amino-acid, which is thus formed, is hydrolysed with hydrochloric acid,



The mono-amino-acids are crystalline and usually decompose when they are strongly heated, with the evolution of carbon dioxide; some of them have a sweet taste. They are neutral to common indicators, and, in fact, may be regarded as *salts*, since the $-\text{COOH}$ and $-\text{NH}_2$ groups of the same or of different molecules neutralise one another, just as do an acid and an amine, with the formation of the ions $-\text{NH}_3^+$ and $-\text{COO}^-$ (compare p. 553). When, therefore, an amino-acid is treated with a strong acid, such as hydrochloric acid, it forms a *hydrochloride*, of which glycine hydrochloride (p. 202) is an example; an amino-acid also forms metallic salts, such as *copper glycine* (p. 202). The *primary* amino-acids are decomposed by nitrous acid, just as are the primary amines, giving the corresponding hydroxy-acids; by measuring the volume of nitrogen evolved the quantity of such an amino-acid in a given solution may be estimated. Amino-acids may also be estimated by treating their solutions with an excess of formalin and then titrating with an alkali, in the presence of which the formaldehyde reacts with the amino-group; the methyleneimino-derivative ($-\text{N}:\text{CH}_2$), which is probably produced, is no longer amphoteric.

Some amino-acids are decomposed by acetic anhydride in the presence of pyridine with the formation of an acetylamino-derivative of a ketone,

$$\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH} + (\text{CH}_3\cdot\text{CO})_2\text{O} = \text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{NHAc})\cdot\text{CO}\cdot\text{CH}_3 + \text{H}_2\text{O} + \text{CO}_2.$$

When heated, α -amino-acids (2 mols.) may condense with the loss of water (2 mols.), giving di-amides (p. 546), analogous to the lactides (p. 254); β -amino-acids (1 mol.) may lose ammonia (1 mol.), giving olefinic acids; γ - and δ amino-acids (1 mol.) may lose water (1 mol.), giving *lactams*, corresponding with the lactones (p. 263).

When an amino-acid is warmed with an aqueous solution of *triketohydrindene hydrate* (*ninhydrin*, p. 491), a deep blue colouration is obtained.

Esters of the amino-acids may be produced by the usual method of esterification—namely, by passing hydrogen chloride into a solution of the acid in excess of an alcohol, and then

decomposing the *hydrochloride* of the ester with a cold solution of an alkali. The esters, unlike the amino-acids, are soluble in ether, &c., so that if the acid solution is treated with alkali and immediately extracted with a suitable solvent, the ester is finally obtained as an oil, which may be purified by distillation under greatly reduced pressure. The esters of the amino-acids, therefore, are of great use; with their aid the amino-acids may be extracted from the products of hydrolysis of a protein, and, to a greater or less extent, separated from one another.

Resolution of dl-amino-acids.—All the amino-acids which are obtained from natural products, with the exception of glycine, are *optically active*, whereas the corresponding *synthetical* compounds, of course, are *dl*-substances. Owing to the amphoteric nature of the amino-acids, they will not, as a rule, form stable salts with either optically active acids or bases, which otherwise might be used for their resolution. They may, however, be separated into their optical isomerides by the following methods: (1) The amino-acid is converted into its *benzoyl*-derivative by the Schotten-Baumann method (p. 453). The amino-group thereby loses its basic character and the *benzoylated* product is a sufficiently strong acid to form stable salts with bases, such as the alkaloids. The *benzoyl*-amino-acid, therefore, may be combined with an optically active base, and the product may then be resolved in the usual way (p. 278). (2) The amino-acid is converted into its ester (above) which is a sufficiently strong base to give, with optically active acids, stable salts which may then be resolved. The *d*- and *l*-*benzoylamino*-acids, or the *d*- and *l*-esters, which are regenerated from their salts, are finally reconverted into the *d*- and *l*-amino-acids respectively, by hydrolysis.

It is thus possible to synthesise many of the *dl*-amino-acids, and then to resolve them into optically active compounds, which are identical with those produced from the proteins.

Ptomaines or Toxines.—Many of the amino-acids are attacked by various putrefactive organisms, giving basic substances, such as putrescine, cadaverine, and neurine (p. 553), which are classed as ptomaines, and some of which are very poisonous. These compounds are formed during the putrefaction of fish, meat, and other animal products which contain proteins, and the toxic action of such putrid matter is partly due to their presence.

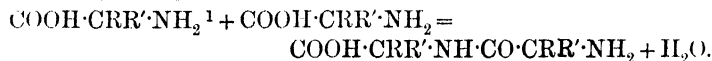
Putrescine, $\text{NH}_2 \cdot [\text{CH}_2]_4 \cdot \text{NH}_2$ (*tetramethylenediamine*), is crystalline, and melts at 27° ; it has a most unpleasant and penetrating smell. It is miscible with water, and is a strong di-acidic base.

Putrescine has been obtained synthetically by converting ethylene dibromide into the dicyanide, and then reducing the latter with sodium and alcohol,



Calaverine, or *pentamethylenediamine*, boils at $178\text{--}179^\circ$, and, like putrescine, is a di-acidic base; its synthesis has already been given (p. 509).

Polypeptides.—A natural protein, as stated above, doubtless consists of a very large number of molecules of the same or of different amino-acids; which have united together with the elimination of water; the first stage in such a condensation of α -amino-acids may be represented by the general equation,

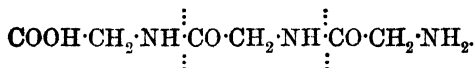


The product so formed from two molecules of an amino-acid is called a *di-peptide*; by condensation with another molecule of the same, or of a different amino-acid, a di-peptide may be transformed into a *tri-peptide*, and so on.

In order to throw light on the nature of the proteins, such condensations were carried out by E. Fischer, and the following methods were used for this purpose: The ethyl ester of glycine undergoes spontaneous decomposition in aqueous solution, giving

a *diamide* of the constitution, $\begin{array}{c} \text{NH} \cdot \text{CH}_2 \cdot \text{CO} \\ | \qquad \qquad | \\ \text{CO} \cdot \text{CH}_2 \cdot \text{NH} \end{array}$, which is called *glycine anhydride* (or *diketopiperazine*). This product is hydrolysed by hot concentrated hydrochloric acid, giving the hydrochloride of *glycyl-glycine*, $\text{COOH} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{NH}_2$.

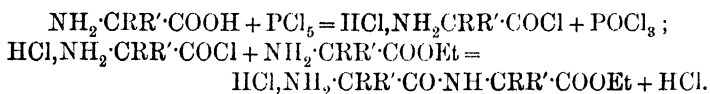
When this *di-peptide*, glycyl-glycine (or its ester), is treated with chloroacetyl chloride, it yields a compound of the constitution, $\text{COOH} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{Cl}$, and the latter, with concentrated ammonia, gives a *tri-peptide*,



¹ R and R' may represent either hydrogen or an alkyl radicle.

The tri-peptide may now be treated with chloroacetyl chloride and ammonia successively, and thus converted into a *tetra-peptide*; and these processes, by which a $-\text{CO}\cdot\text{CH}_2\cdot\text{NH}_2$ group is substituted for an atom of hydrogen of an amino-group, may be continued.

In another method, the amino-acid is treated with phosphorus pentachloride and acetyl chloride, and the acid chloride, which is thus produced, in the form of its hydrochloride, is then caused to react with an ester of an amino-acid,



The product is then made the starting-point of further condensations.

The most complex substance produced by E. Fischer, by methods such as those just indicated, is an *octadecapeptide*, the molecule of which contains 15 glycol- or $-\text{NH}\cdot\text{CH}_2\cdot\text{CO}-$ and three *leucyl*- or $-\text{NH}\cdot\text{CH}(\text{C}_4\text{H}_9)\cdot\text{CO}-$ groups (p. 549); this compound has a molecular weight of 1212, and its constitution is expressed by the formula, $\text{NH}_2\cdot\text{CH}(\text{C}_4\text{H}_9)\cdot\text{CO}[\text{NH}\cdot\text{CH}_2\cdot\text{CO}]_3\cdot\text{NH}\cdot\text{CH}(\text{C}_4\text{H}_9)\cdot\text{CO}\cdot[\text{NH}\cdot\text{CH}_2\cdot\text{CO}]_3\cdot\text{NH}\cdot\text{CH}(\text{C}_4\text{H}_9)\cdot\text{CO}\cdot[\text{NH}\cdot\text{CH}_2\cdot\text{CO}]_8\cdot\text{NH}\cdot\text{CH}_2\cdot\text{COOH}$. It is in many respects similar to the natural proteins, and gives the colour reactions of those substances: like the latter it does not diffuse through a parchment membrane and is precipitated from its solutions by tannic acid, &c. (p. 473). It seems, nevertheless, that proteins are not merely open-chain polypeptides of high molecular weight, since pepsin, which hydrolyses proteins (p. 575) has little, if any, action on synthetic polypeptides; on the other hand, the graded hydrolysis of proteins gives certain polypeptides, identical with some of those which have been prepared synthetically.

Classification of Amino-Acids.—The more important amino-acids obtained from proteins are of various types and may be conveniently classified as follows:

Mono-amino-derivatives of aliphatic mono-carboxylic acids:

Glycine, *d*-Alanine, *l*-Serine, *d*-Valine, *l*-Leucine, *d*-Iso-leucine.

Di-amino-derivatives of aliphatic mono-carboxylic acids:

d-Arginine, *d*-Lysine.

Mono-amino-derivatives of aliphatic di-carboxylic acids:
l-Aspartic acid, *d*-Glutamic acid, *d*-Hydroxyglutamic acid.

Aromatic amino-acids: *l*-Phenylalanine, *l*-Tyrosine.

Heterocyclic amino-acids: *l*-Histidine, *l*-Tryptophane, *l*-Proline, *l*-Hydroxyproline.

The above-named compounds, together with the thio-amino-acids (*l*-cystine and *l*-methionine), all of which are obtained from proteins, are briefly described below; a short account of certain alkyl-amino-acids and related compounds which are obtained from animals, but which are not products of protein hydrolysis, is also given.

Amino-Mono-Carboxylic Acids.

Glycine (aminoacetic acid), the simplest amino-acid which is obtained from proteins, has already been described (p. 202); it forms about 25 per cent. of the products of hydrolysis when glue or gelatin is decomposed with dilute sulphuric acid.

d-**Alanine**, $\text{CH}_3\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (*α -aminopropionic acid*), is one of the principal products of the hydrolysis of fibroin (the main component of silk) and has been obtained synthetically by the methods already described. It decomposes at about 297° , and with nitrous acid, it gives *d*-lactic acid.

dl-**Alanine** and its structural isomeride, *β -aminopropionic acid*, $\text{NH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{COOH}$, may be prepared by treating the corresponding bromopropionic acids with ammonia.

l-**Serine**, $\text{HO}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (*β -hydroxy- α -aminopropionic acid*), easily racemises, so that although it may be a component of many proteins, the *dl*-compound is obtained when silk-fibroin, casein, &c., and related substances, such as gelatin and keratin, are decomposed with acids; the *dl*-acid decomposes at 246° and has a sweet taste.

l-**Cystine**, $\text{COOH}\cdot\text{CH}(\text{NH}_2)\cdot\text{CH}_2\cdot\text{S}\cdot\text{S}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$, is a derivative of alanine and is formed in small quantities by the hydrolysis of several proteins, of which it is the chief sulphur-containing compound; it is sometimes present in urinary sediments and also in certain gall-stones. The *dl*-acid may be obtained by the atmospheric oxidation of *α -amino- β -thiohydroxypropionic acid*, $\text{HS}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (or *cysteine*) in alkaline

solution. It is sparingly soluble in cold water and decomposes at about 260° .

***l*-Methionine**, $\text{CH}_3\cdot\text{S}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$, a methyl derivative of the next homologue of *l*-cysteine, has also been obtained from proteins.

***d*-Valine**, $\text{CHMe}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (*α -aminoisovaleric acid*), is an important product of the hydrolysis of casein, zein (the protein of wheat and maize), and edestin (from hemp seed).

***l*-Leucine**, $(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (*α -aminoisocaproic acid*), is very widely distributed in the animal kingdom, and is a substance of great physiological importance. It is found in the lymphatic glands, the spleen, and especially in the pancreas; in typhus and some other diseases it is present in considerable quantity in the liver. It is produced during the putrefaction or the hydrolysis of many proteins, especially hæmoglobin (p. 575), milk-albumin, and casein (p. 576), from the last of which it may be prepared.

Leucine crystallises in glistening plates, melts at 270° , and is sparingly soluble in water; when carefully heated it sublimes unchanged, but when rapidly heated it decomposes into isoamylamine, $\text{CHMe}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2$, and carbon dioxide. It undergoes atmospheric oxidation in aqueous solution in the presence of charcoal, giving isovaleric acid, carbon dioxide, and ammonia, $\text{CHMe}_2\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH} + \text{O}_2 = \text{C}_4\text{H}_9\cdot\text{COOH} + \text{CO}_2 + \text{NH}_3$. Its aqueous solution is laevorotatory, but that of its hydrochloride shows dextro-rotation; when boiled with baryta-water leucine racemises (p. 276).

dl-Leucine has been prepared synthetically from isovaleraldehyde (p. 544), and in the form of its benzoyl- or formyl-derivative, it has been resolved into its components; the *l*-leucine obtained in this way is identical with that prepared from proteins.

***d*-Isoleucine**, $\text{CHMeEt}\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (*α -amino- β -methylvaleric acid*), is produced by the hydrolysis of proteins contained in beetroot-sap, cereals, potatoes, &c., and when these materials are used for the preparation of alcohol, the *d*-isoleucine, which is first produced, is afterwards converted into active amyl alcohol by the action of the enzymes which are present. *l*-Leucine, under similar conditions, gives rise to isobutylcarbinol (p. 111).

Di-Amino-Mono-Carboxylic Acids.

***d*-Arginine**, $\text{NH}_2 \cdot \text{C}(\text{:NH}) \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$, is an important compound, derived from $\alpha\delta$ -diamino-*n*-valeric acid, and is formed by the hydrolysis of many proteins; a polypeptide or *protamine* (*salmine*) obtained from Rhine salmon gives as much as 87 per cent. of arginine. On hydrolysis with a solution of barium hydroxide, arginine gives urea and ***d*-ornithine**, $\text{NH}_2 \cdot [\text{CH}_2]_3 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$ ($\alpha\delta$ -diaminovaleric acid).

***d*-Lysine**, $\text{NH}_2 \cdot [\text{CH}_2]_4 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$ ($\alpha\epsilon$ -diaminocaproic acid), occurs among the hydrolytic products of casein, egg-albumin, and other proteins. In the putrefactive decomposition of proteins ornithine gives tetramethylenediamine, and lysine gives pentamethylenediamine (p. 546).

Mono-Amino-Di-Carboxylic Acids.

***L*-Aspartic acid**, $\text{COOH} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$ (*aminosuccinic acid*) is formed by the hydrolysis of many proteins; with nitrous acid it gives *L*-malic acid (p. 254). Unlike aminomonocarboxylic acids, *L*-aspartic acid and other members of this group, have well-marked acidic properties.

***L*-Asparagine**, $\text{NH}_2 \cdot \text{CO} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$, a mono-amide of *aminosuccinic acid* (aspartic acid), occurs in many plants, particularly in asparagus, and in the young shoots of beans, peas, and lupines, from which it may be obtained by extraction with water. It is readily soluble in water, sparingly soluble in alcohol and ether. When heated with acids or alkalis, it is converted into *L*-aspartic acid.

***d*-Asparagine** also occurs, together with *L*-asparagine, in the young shoots of lupines; it has a sweet taste, but that of *L*-asparagine is very unpleasant.

It is noteworthy that when an aqueous solution of equal quantities of *d*- and *L*-asparagine is evaporated, hemihedral crystals of the two active modifications are deposited side by side; a racemic compound is not formed (compare p. 272).

***d*-Glutamic acid**, $\text{COOH} \cdot \text{CH}(\text{NH}_2) \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{COOH}$ (α -amino-glutaric acid), occurs in the sprouting seeds of various plants, and is an important product of the hydrolysis of casein and of gliadin, the protein of wheat and rye, which gives more than 40

per cent. of the acid; it forms lustrous crystals which decompose at about 202° .

d-Hydroxyglutamic acid, a β -hydroxy-derivative of *d*-glutamic acid is also produced by the hydrolysis of casein and other proteins.

Aromatic Amino-Acids.

***l*-Phenylalanine**, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$ (β -phenyl- α -aminopropionic acid), is formed by the hydrolysis of cheese, egg-albumin, gelatin, &c.; the *dl*-acid has been synthesised as described below and has been resolved into its *d*- and *l*-components.

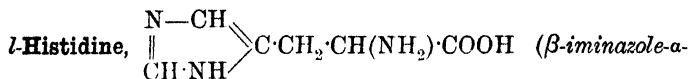
***l*-Tyrosine**, $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$, or β -*p*-hydroxyphenyl- α -aminopropionic acid, is formed in the decomposition of many proteins. It is found in the liver in some diseases, in the spleen, pancreas, and in cheese (its name is derived from τυρος, cheese). It was first prepared by fusing cheese with potash (Liebig, 1846). Tyrosine is sparingly soluble in water, and with mercuric nitrate in aqueous solution, it gives a yellow precipitate, which, when boiled with dilute nitric acid, acquires an intense red colour.

Tyrosine melts at about 316° and decomposes into carbon dioxide and *p*-hydroxyphenylethylamine, $\text{HO}\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{NH}_2$.

Tyrosine has been synthesised in the following way: Phenylacetaldehyde (p. 462) yields, with hydrocyanic acid, the nitrile of phenyllactic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{OH})\cdot\text{CN}$, which, with alcoholic ammonia, gives the nitrile of phenylaminopropionic acid, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{CN}$; this nitrile, on hydrolysis, yields phenylaminopropionic acid (phenylalanine), $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$.

Nitric acid converts this amino-acid into *p*-nitrophenylaminopropionic acid, $\text{NO}_2\cdot\text{C}_6\text{H}_4\cdot\text{CH}_2\cdot\text{CH}(\text{NH}_2)\cdot\text{COOH}$, from which, on reduction, the corresponding aminophenylaminopropionic acid is obtained; the latter, on treatment with nitrous acid, yields *dl*-tyrosine.

Heterocyclic Amino-Acids.



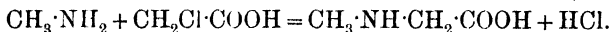
***l*-Histidine**, was first found among the products of hydrolysis of *sturgeon*, a polypeptide obtained from the sturgeon, and is formed from many proteins; it decomposes at about 253° .

***l*-Tryptophane**, $\text{NH} \begin{smallmatrix} \text{CH} \\ \diagup \text{C}_6\text{H}_4 \diagdown \end{smallmatrix} \text{C} \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$ (*β -indole- α -aminopropionic acid*), is a decomposition product of egg- and blood-albumin, and under the influence of putrefactive bacteria, it is converted into *aminoethylindole*, $\text{NH} \begin{smallmatrix} \text{CH} \\ \diagup \text{C}_6\text{H}_4 \diagdown \end{smallmatrix} \text{C} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{NH}_2$.

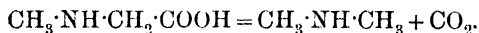
***l*-Proline**, $\begin{array}{c} \text{CH}_2 - \text{CH}(\text{COOH}) \\ | \\ \text{CH}_2 - \text{CH}_2 \end{array} \begin{smallmatrix} > \text{NH} \end{smallmatrix}$ (*pyrrolidine- α -carboxylic acid*), occurs among the products of hydrolysis of gliadin, salmine, gelatin, casein, &c.; ***l*-hydroxyproline**, $\begin{array}{c} \text{CH}_2 - \text{CH}(\text{COOH}) \\ | \\ \text{HO} - \text{CH} - \text{CH}_2 \end{array} \begin{smallmatrix} > \text{NH} \end{smallmatrix}$, also occurs among the products of the hydrolysis of gelatin.

Alkylamino-Acids and Related Compounds.

Sarcosine, $\text{CH}_3 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOH}$ (*methylglycine*), was first obtained (Liebig, 1847) by boiling creatine with baryta-water (p. 554); it is also formed when caffeine is similarly treated, but apparently it is not produced by the hydrolysis of proteins. It may be prepared synthetically from chloroacetic acid and methylamine,



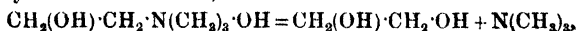
Sarcosine melts and decomposes at 210–220°, giving dimethylamine and carbon dioxide,



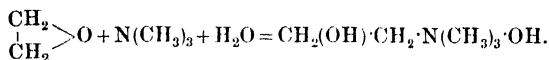
Choline, $\text{CH}_2(\text{OH}) \cdot \text{CH}_2 \cdot \text{N}(\text{CH}_3)_3 \cdot \text{OH}$ (*hydroxyethyltrimethylammonium hydroxide*), is an alcohol related to betaine (p. 553). It is one of the products of the hydrolysis of lecithin (p. 564), and is widely distributed in the animal and vegetable kingdoms. It was discovered by Strecker in bile ($\chi\omicron\lambda\eta$), and its constitution was established by Baeyer. Choline is contained in hops, and also in the alkaloid, sinapine, which occurs in mustard-seeds; it is produced in corpses, as the result of putrefactive changes.

Choline is a strongly alkaline liquid, miscible with water; a characteristic salt is the *platinichloride*, $(\text{C}_5\text{H}_{14}\text{ON})_2\text{PtCl}_6$, which crystallises from water in plates.

When a strong aqueous solution of choline is boiled, glycol and trimethylamine are formed,



a decomposition which clearly shows the constitution of the substance. Choline was first synthesised by Wurtz, who obtained it by evaporating an aqueous solution of ethylene oxide with trimethylamine,



Neurine, $\text{CH}_2 \cdot \text{CH} \cdot \text{N}(\text{CH}_3)_3 \cdot \text{OH}$ (*vinyltrimethylammonium hydr-oxide*), is formed when choline is heated with baryta-water, and it is also a decomposition product of lecithin, from which it is doubtless produced by bacterial action after death. It is exceedingly poisonous, and is one of the important ptomaines (p. 545).

Betaine, $\text{COOH} \cdot \text{CH}_2 \cdot \text{N}(\text{CH}_3)_3 \cdot \text{OH}$ (*oxynneurine* or *lycine*), may be regarded as a derivative of sarcosine, or of glycine. It occurs in beetroot (*Beta vulgaris*), and is obtained in large quantities as a by-product in the manufacture of beet-sugar; it is also found in some seeds, especially in those of the cotton-plant.

Betaine is very soluble in water, and can be obtained in deliquescent crystals, which may represent the hydroxy-acid, but at 100° , it loses the elements of water and is converted into a salt, $\text{N}(\text{CH}_3)_3 \cdot \text{CH}_2 \cdot \text{CO} \cdot \bar{\text{O}}$.

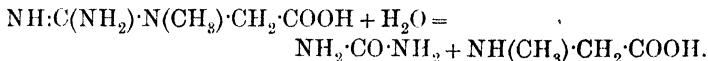
This salt, also called betaine, melts at 293° , undergoing isomeric change into methyl dimethylaminoacetate, $\text{N}(\text{CH}_3)_2 \cdot \text{CH}_2 \cdot \text{COOMe}$. Corresponding derivatives of other α -, β -, and γ -amino-acids also lose a molecule of water giving inner salts, or *betaines* of the type shown above.

Muscarine occurs in the fungus, Fly Agaric (*Amantia muscaria*), which is highly toxic to flies. It is a strong base, and is very poisonous to man, acting especially on the heart. Its constitution is not settled.

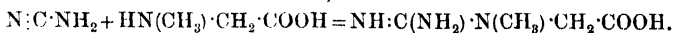
Creatine, $\text{NH} \cdot \text{C}(\text{NH}_2) \cdot \text{N}(\text{CH}_3) \cdot \text{CH}_2 \cdot \text{COOH}$, is a very important substance found in the muscles, nerves, and blood, and also in considerable quantity in meat extract, from which it was isolated by Chevreul in 1843. The muscles contain about 0.4 per cent. of creatine, and it has been calculated that those of a full-grown man contain no less than 90–100 grams of this substance. The name creatine is derived from *κρεας*, flesh.

Creatine crystallises from water in hydrated prisms ($1\text{H}_2\text{O}$); it is moderately soluble in water, very sparingly soluble in alcohol. It has a neutral reaction and a bitter taste, and forms salts with

1 equivalent of an acid, but it does not appear to possess acidic properties. When evaporated with acids it is converted into *creatinine* (see below), and when heated with baryta-water, it is decomposed into urea and *sarcosine*,



Creatine has been synthesised by heating together cyanamide (p. 319) and sarcosine in alcoholic solution,



Creatinine, $\text{NH}\cdot\text{C} \begin{array}{l} \text{NH} \text{---} \text{CO} \\ \diagup \quad \diagdown \\ \text{N}(\text{CH}_3)\cdot\text{CH}_2 \end{array}$, can be prepared from creatine, into which it is reconverted by alkalis. It is found (about 0.13 per cent.) in urine, and is also present in the muscles, especially after great exertion; in both these cases it may be produced from creatine.

Creatinine is much more soluble in water than is creatine; it is a strong base, and yields salts, such as the hydrochloride, $\text{C}_4\text{H}_7\text{ON}_3\cdot\text{HCl}$. When zinc chloride is added to its aqueous solution, a highly characteristic, sparingly soluble compound, $(\text{C}_4\text{H}_7\text{ON}_3)_2\cdot\text{ZnCl}_2$, separates in fine needles, and this compound is used in the estimation of creatinine. Creatinine reduces Fehling's solution, and gives with phosphomolybdic acid a yellow, crystalline precipitate.

CHAPTER XXXVIII.

URIC ACID AND OTHER PURINE DERIVATIVES.

THE principal compounds described in this chapter are closely related in structure and are classed as the *purine* derivatives (p. 559). Some of them occur in the vegetable kingdom or in the animal kingdom only; others are found in both. Uric acid and other purine derivatives of animal origin are formed in the human body by the decomposition or degradation of the highly complex proteins (p. 572).

Uric acid, $\text{C}_5\text{H}_4\text{O}_3\text{N}_4$, occurs in human urine, which, on exposure to the air, deposits the acid as a light yellow powder; sometimes uric acid gradually accumulates in the bladder, form-

ing large masses (stones), or is deposited in the tissues of the body (gout and rheumatism). It was discovered (in 1776) by Scheele in urinary calculi. It also occurs in large quantities as ammonium urate in the excrement of birds (*guano*) and reptiles, and is conveniently prepared by boiling the excrement with caustic soda, until all the ammonia has been expelled, and then pouring the hot filtered liquid into hydrochloric acid; the uric acid gradually separates as a fine crystalline powder.

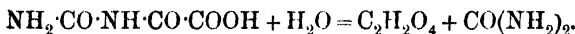
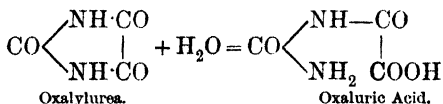
Uric acid is practically insoluble in alcohol and ether, and very sparingly so in water (1 part dissolves in 88,000 parts of water at 18°, and in 1800 parts at 100°).

It behaves like a weak dibasic acid; with sodium carbonate solution it yields a sodium hydrogen salt, $C_5H_3O_3N_4Na, \frac{1}{2}H_2O$, but with sodium hydroxide solution it gives the normal sodium salt, $C_5H_2O_3N_4Na_2, H_2O$. The metallic hydrogen salts, like the acid itself, are all very sparingly soluble in water, but the lithium hydrogen salt is more soluble (1 in 368 parts at 19°) than those of the other alkali metals, and for this reason lithium carbonate is used in medicine, in cases of gout and rheumatism.

Test for Uric Acid.—When uric acid (say 0.05 g.) is evaporated to dryness in a porcelain basin with a few drops of concentrated nitric acid, it gives first a yellow and then a reddish-pink residue, which dissolves in ammonia, forming a purple-red solution (murexide reaction). When it is heated alone, uric acid decomposes, giving ammonia, carbon dioxide, urea, cyanuric acid, and other products.

The first important evidence as to its structure was obtained by a study of the oxidation products of the acid; when treated with nitric acid under suitable conditions, it yields *oxalylurea*, *mesoxalylurea*, and *urea*.

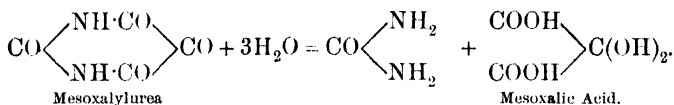
Oxalylurea (*parabanic acid*), $C_3H_2O_3N_2$, is a crystalline substance, soluble in water and alcohol; it yields a silver derivative, $C_3O_3N_2Ag_2$, and thus behaves like a dibasic acid. When treated with baryta-water, it is hydrolysed in two stages, yielding first *oxaluric acid*, and then oxalic acid and urea,



The constitution of *oxalylurea* is further established by the synthesis of the compound from a mixture of oxalic acid and urea, in the presence of phosphorus oxychloride.

Mesoxalylurea (*alloxan*), $C_4H_2O_4N_2$, crystallises from water in hydrated prisms, $(4H_2O)$. In contact with the skin its aqueous solution produces, after some time, a purple stain; ferrous salts colour the aqueous solution indigo-blue.

When boiled with alkalis, it is converted into urea and a salt of *mesoxalic acid*,¹



Oxalylurea (*parabanic acid*) and mesoxalylurea (*alloxan*) are classed as *ureides*, a term which is applied to acyl-derivatives of urea, such as *acetylurea*, $NH_2 \cdot CO \cdot NH \cdot CO \cdot CH_3$, and *diacetylurea*, $CO(NH \cdot CO \cdot CH_3)_2$. The more important ureides, however, are those derived from urea by the displacement of one of the hydrogen atoms of both the NH_2 - groups by a bivalent acid radical, and in addition to the two examples given above the derivatives of malonic acid are of interest.

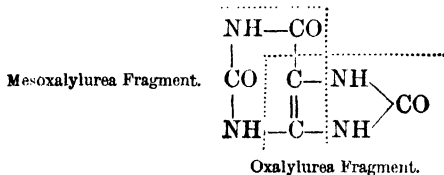
Malonylurea (*barbituric acid*), $CO \begin{array}{c} \swarrow \text{NH} \cdot \text{CO} \\ \searrow \text{NH} \cdot \text{CO} \end{array} CH_2$, may be prepared by heating a mixture of urea and malonic acid with phosphorus oxychloride at 100° , and also by boiling an alcoholic solution of urea with ethyl sodiomalonate; it crystallises from water in prisms $(2H_2O)$, and from its solution in ammonia, silver nitrate precipitates a *silver* derivative, $C_4H_2O_3N_2Ag_2$. Numerous alkyl derivatives of malonylurea, prepared from urea and alkyl substitution products of ethyl malonate, are used as soporifics or anæsthetics, as, for example, *diethylmalonylurea* (*veronal*) the *sodium ethyl* derivative of *methylbutylmalonylthiourea* (*pentothal*), and *N-methyl-cyclohexenylmethylmalonylurea* (*evipan*).

It will be seen from the formulæ of the ureides of dicarboxylic acids that the molecules of these compounds, like those of succinimide (p. 248) and phthalimide (p. 458) contain imido-groups.

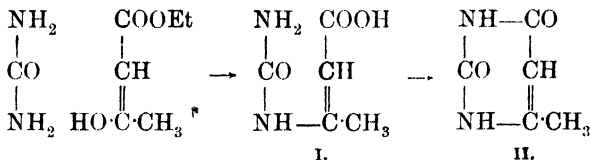
¹ *Mesoxalic acid*, or *dihydroxymalonic acid*, is formed when dibromomalonic acid, $CBr_2(COOH)_2$, is boiled with baryta-water; it melts at 108° , and is one of the few compounds in the molecule of which there is a group, $>C(OH)_2$, stable at 100° .

$-\text{CO}\cdot\text{NH}\cdot\text{CO}-$; as the hydrogen atom of such a group is displaceable by metals, and the ureides thus formed salts, some of them were given names such as parabanic acid, barbituric acid, &c., before their structures were known. Uric acid, and other members of the purine group (p. 559) which give metallic salts, are also imides and not carboxylic acids. It is not easy to decide whether the molecules of these salt-forming ureides contain the lactam group $-\text{CO}\cdot\text{NH}-$, or the tautomeric lactim $-\text{C}(\text{OH})\text{:N}-$ complex, and either formulation may be used, but it is known that when the metallic salts react with methyl iodide, the methyl group or groups in the products are combined with nitrogen. The first product of hydrolysis of a ureide of this type, such as oxalylurea, is called a ureido-acid, as, for example, oxaluric acid (p. 555).

Syntheses of Uric Acid.—The constitutions and relationships of the above, and of other *degradation* products of uric acid, having been established—mainly by Baeyer—the following structural formula for the acid was suggested by Medicus in 1875:¹



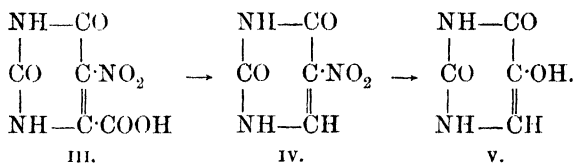
This formula, which was based on the formation of the three oxidation products, oxalylurea, mesoxalylurea, and urea, was finally established by the synthesis of uric acid by Behrend and Roosen in the following manner: Ethyl acetoacetate (in the enolic form, p. 189) condenses with urea, giving *ethyl β-uramidocrotonate*; and the corresponding acid, *β-uramidocrotonic acid*, i.,



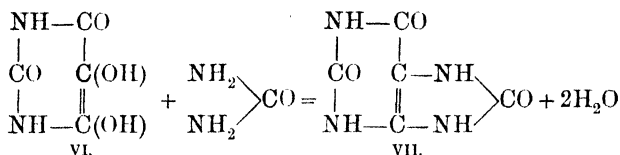
which is obtained by hydrolysis, readily loses water and forms *methyluracil*, II. When methyluracil is treated with nitric acid,

¹ The structures of uric acid and its derivatives are given in the form used by Medicus, Baeyer, Fischer and others.

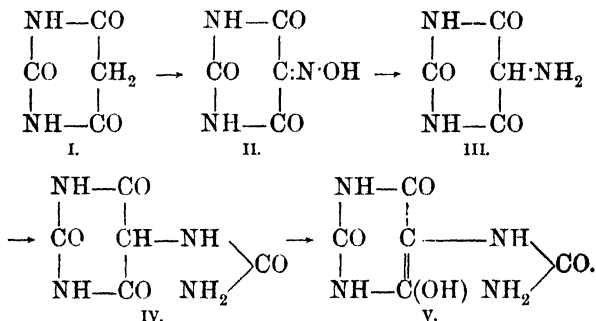
the methyl- is oxidised to a carboxyl-group, and at the same time a nitro-group is substituted for an atom of hydrogen. The *nitro-uracilic acid*, III., which is thus obtained, is decomposed in boiling alkaline solution, giving *nitrouracil*, IV., which, when treated with tin and hydrochloric acid, is converted into a mixture of *aminouracil* and *hydroxyuracil*, V.



Bromine-water oxidises hydroxyuracil to *dihydroxyuracil* or *dialuric acid*, VI., which, when heated with urea and sulphuric acid, yields uric acid, VII.,



A later synthesis of uric acid was carried out as follows: *Malonyl-urea* (*barbituric acid*), I. (p. 556), prepared by heating urea with malonic acid, is treated with nitrous acid, by which it is converted into *violuric acid*, II. On reduction, this acid gives *uramil*, III., which reacts with potassium cyanate in aqueous solution to form *pseudouric acid*, IV.:

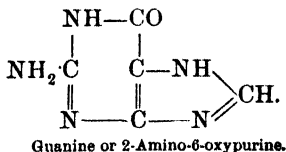
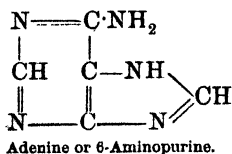
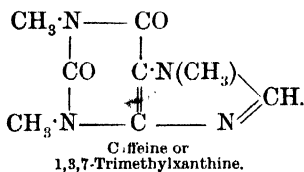
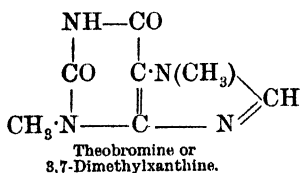
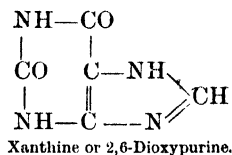
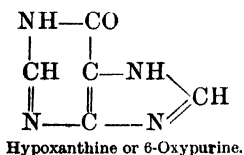
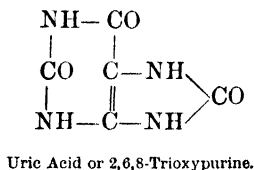
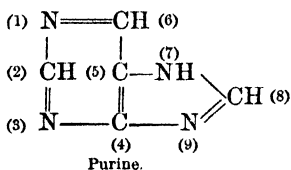


When this acid is melted with oxalic acid, or heated with hydro-

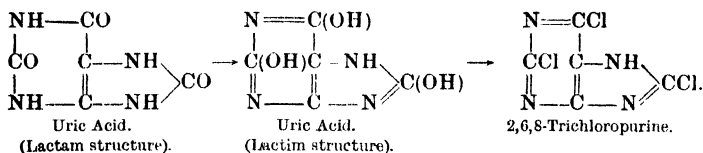
chloric acid, it loses the elements of water and gives uric acid; in this last stage (accomplished by E. Fischer) the pseudouric acid probably first undergoes a tautomeric change into the enolic form, v.

Methyluric Acids.—When an alkaline solution of uric acid is shaken with an excess of methyl iodide, mono-, di-, tri-, and finally a tetramethyluric acid, are formed; in all these compounds, the methyl groups are directly combined with nitrogen.

The Purine Derivatives.—Uric acid, and many other important natural products, may be regarded as derived from *purine*; this compound and many related substances were prepared by E. Fischer. The names and formulæ of the more important members of the purine group are given below, numbers being used to indicate the positions of the substituents, as shown in the formula of the parent substance:



Purine, $C_5H_4N_4$, may be obtained from uric acid by first heating the acid at about 160° with a large excess of phosphorus oxychloride, which converts it into 2,6,8-trichloropurine; in this transformation the uric acid reacts as if it were a trihydroxy-compound (2,6,8-trihydroxypurine) or tri-lactim, since three atoms of hydrogen and three atoms of oxygen are displaced by three atoms of chlorine:



The 2,6,8-trichloropurine thus obtained, treated with hydriodic acid at 0° , is converted into 2,6-diiodopurine, and this compound, with zinc-dust and water, is reduced to purine.

Purine melts at 216° , and is very readily soluble in water; it has both basic and acidic properties.

Hypoxanthine, $C_5H_4ON_4$ (*sarkine*, or 6-oxypurine), has been found, usually accompanied by xanthine, in the blood and in urine; also in the muscles, spleen, liver, pancreas, and marrow. It is sparingly soluble in water, but dissolves readily in both acids and alkalis; it may be obtained from adenine, as described later.

Xanthine, $C_5H_4O_2N_4$ (2,6-dioxypurine), occurs in small quantities in the blood, the liver, the urine, and in urinary calculi; it is also present in tea. It may be obtained by treating guanine (p. 562) with nitrous acid; the hydroxy-compound (lactim) thus formed, or the corresponding lactam, is identical with xanthine.

Xanthine may also be obtained from uric acid, since 2,6,8-trichloropurine (see above) with sodium ethoxide, gives 2,6-diethoxy-8-chloropurine, which is converted into xanthine by hydriodic acid.

Xanthine is a colourless amorphous powder, sparingly soluble in water, but readily soluble in alkalis; it gives a lead derivative, which, when heated with methyl iodide, yields *theobromine*. When oxidised with potassium chlorate and hydrochloric acid, it is resolved into urea and mesoxalylurea (p. 556).

Theobromine, $C_7H_8O_2N_4$ (3,7-dimethylxanthine), occurs in cocoa-beans, and resembles caffeine in properties; when treated with an

ammoniacal solution of silver oxide, it yields *silver theobromine*, which reacts readily with methyl iodide, giving caffeine.

Theophylline, $C_7H_8O_2N_4$ (*1,3-dimethylxanthine*), an isomeride of theobromine, occurs in tea and melts at 264° .

Caffeine, $C_8H_{10}O_2N_4$ (*theine*, *1-methyltheobromine*, or *1,3,7-trimethylxanthine*), occurs in coffee-beans (1-1.5 per cent.), in tea (2-5 per cent.), in kola-nuts (1-2 per cent.), and in other vegetable products.

Tea (1 part) is macerated with hot water (4 parts), milk of lime (1 part) is added, and the mixture is evaporated to dryness on a water-bath; the caffeine is then extracted by means of chloroform, the extract is evaporated, and the crude base is purified by recrystallisation from water.

✓ Caffeine forms colourless needles, $(1H_2O)$, melts at 239° , and at higher temperatures sublimes unchanged; it has a bitter taste, and is sparingly soluble in cold water and alcohol. It is a feeble base, and forms salts with strong acids only; even the *hydrochloride*, $C_8H_{10}O_2N_4 \cdot HCl$, is hydrolysed by water. Caffeine is a nerve stimulant and also a diuretic; its salts, generally the *citrate*, are used in medicine.

✎ *Tests for Caffeine*.—When caffeine (say 0.05 g.) is evaporated with concentrated nitric acid (1-2 drops) in a porcelain basin, it gives a yellow residue, which, after having been heated over the free flame until it has turned brown, gives a purple-red solution with ammonia (compare murexide reaction, p. 555). A solution of caffeine (0.05 g.) in chlorine-water (about 5 c.c.) yields, on evaporation, a yellowish-brown residue, which dissolves in dilute ammonia, giving a purple solution.

✓ Caffeine may be obtained from uric acid in various ways, as, for example, by the following stages: Uric acid \rightarrow trichloropurine \rightarrow diethoxychloropurine \rightarrow xanthine \rightarrow theobromine \rightarrow caffeine. A simpler method, which has been employed commercially, is to convert uric acid into tetramethyluric acid (p. 559), which with phosphorus oxychloride at 160° gives chlorocaffeine, a methyl group being displaced by chlorine; on reduction with hydriodic acid the chloro-derivative gives caffeine.

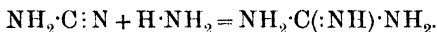
Adenine, $C_5H_5N_5$ (*6-aminopurine*), may be prepared from the nuclei of cells, and is thus often found in the extracts of animal tissues. It crystallises from water in pearly plates $(3H_2O)$. Nitrous acid converts it into *hypoxanthine*, the amino- being displaced by a hydroxyl-group (compare xanthine, p. 560). It

has been obtained synthetically from trichloropurine (p. 560), which, when treated with ammonia, gives 6-amino-2,8-dichloropurine; the latter, on reduction with hydriodic acid, gives adenine.

Guanine, $C_5H_5ON_5$ (2-amino-6-oxypurine), has been found in guano, the liver, the pancreas, and in animal tissues. It can be obtained from 2,6,8-trichloropurine, which, when heated with alkalis, gives 6-oxo-2,8-dichloropurine; this compound is converted into 8-chloroguanine with alcoholic ammonia, and the product, reduced with hydriodic acid, gives guanine. It is an amorphous powder, which combines with acids to form crystalline salts. When treated with nitrous acid, it yields xanthine (p. 560), and on oxidation, it gives oxalylurea (p. 555) and guanidine.

In the animal body guanine is transformed into xanthine, and adenine into hypoxanthine, which is then converted into xanthine; the last-named compound is further oxidised to uric acid. With the exception of uric acid, these purine bases also occur in the vegetable kingdom, especially in germinating seeds.

Guanidine, $NH_2 \cdot C(:NH) \cdot NH_2$ (*iminourea*), is not a purine derivative, and was first prepared by Strecker in 1861 by the oxidation of guanine with potassium chlorate and hydrochloric acid. It may be synthesised by treating cyanogen iodide¹ with ammonia, cyanamide (p. 319) being formed as an intermediate product,



Guanidine is conveniently prepared by heating ammonium thiocyanate at 170–200°, when the thiourea (p. 320), which is first produced, reacts with a further quantity of the ammonium thiocyanate, yielding guanidine thiocyanate,

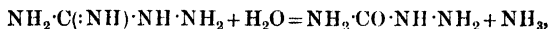


Guanidine forms colourless crystals, and is readily soluble in water; it is a strong mono-acidic base, and of its salts the nitrate, $NH_2 \cdot C(:NH) \cdot NH_2, HNO_3$, like urea nitrate, is sparingly soluble in water. The base is decomposed by a solution of barium hydroxide, giving urea and ammonia.

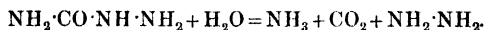
When guanidine is treated with a mixture of nitric and sulphuric acids, it yields *nitroguanidine*, $NH_2 \cdot C(:NH) \cdot NH \cdot NO_2$, which, on re-

¹ Cyanogen iodide sublimes in colourless needles when a mixture of iodine and mercuric cyanide is heated; it is very poisonous.

duction with zinc-dust and acetic acid, is converted into *aminoguanidine*, $\text{NH}_2\cdot\text{C}(\text{:NH})\cdot\text{NH}\cdot\text{NH}_2$. When the latter is warmed with acids, it yields *semicarbazide*,



which may be further hydrolysed into ammonia, carbon dioxide, and *hydrazine*,



Semicarbazide is an important reagent (p. 138).

CHAPTER XXXIX.

SOME IMPORTANT COMPONENTS OF ANIMALS AND PLANTS.

THE cells of plants and of animals, even those of the lowest organisms, are wonderful laboratories, in which compounds of great complexity are synthesised from very simple materials—and are also decomposed again—by chemical processes, many of which it is as yet impossible to bring about without the aid of the living organism, or at least of those little-known agents, the enzymes (p. 303), which are formed in the living cells. Plants absorb carbon dioxide from the air, dissolved mineral matter—which must include nitrates or ammonium salts—from the soil, and produce carbohydrates, fats, and proteins (p. 572), which serve as food for animals; in addition, vegetable organisms synthesise a very large number of other most important substances, such as the alkaloids and purines, oil of turpentine, and other terpenes, essential oils, rubber, resins, many colouring matters, glucosides, &c. Animals cannot synthesise the components of their bodies from the simple materials which are adequate to plants; they must be supplied with carbohydrates, fats, and proteins from which they, in their turn, elaborate a great variety of compounds essential to their life.

In this chapter a few of the more notable and interesting components of living matter are described briefly; many of them are of great complexity and their structures are still unknown, but substantial progress has already been made in many directions, with results of the utmost importance to mankind.

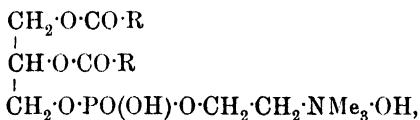
Lecithin is very widely distributed throughout the animal and

vegetable kingdoms. It is found in small quantities in bile and in most organs of the body, and is especially prominent in the brain-substance and nerve tissues, the blood corpuscles, and the liver; it occurs in considerable quantities in yolk of egg (hence its name, from *λεχιθος*, yolk of egg), and is also found in plants, particularly in the seeds.

Lecithin is a waxy, apparently crystalline, very hygroscopic substance, readily soluble in alcohol and ether; in contact with water, it swells up and forms an opalescent, colloidal solution.

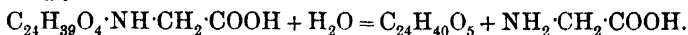
It is dextrorotatory, but is readily racemised. When hydrolysed it gives choline (p. 552), two or more (saturated or unsaturated) monocarboxylic acids, such as stearic, palmitic, or oleic acid, and glycerophosphoric acid,¹ or its decomposition products.

The constitution of lecithin may, therefore, be represented by the formula,



in which $-\text{CO} \cdot \text{R}$ represents the radical of one of the acids just mentioned, or that of some other monocarboxylic acid. Many varieties of lecithin occur in animals and plants, differing from one another as regards the organic acids which they give on hydrolysis. A more complex substance, *protagon*, obtained from brain-tissue, which seemed to be closely related to the lecithins, is now known to be a mixture.

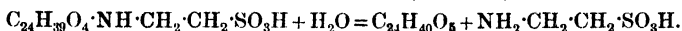
Glycocholic acid, $\text{C}_{24}\text{H}_{39}\text{O}_4 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{COOH}$, occurs in human bile in the form of its sodium salt, $\text{C}_{26}\text{H}_{42}\text{O}_6 \cdot \text{NNa}$. It forms colourless needles, melts at 133° , and is soluble in water and alcohol, but very sparingly so in ether; its alcoholic solution is dextrorotatory. When boiled with alkalis, it yields *cholic acid* and glycine,



Taurocholic acid, $\text{C}_{24}\text{H}_{39}\text{O}_4 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{SO}_3\text{H}$, also occurs in human bile and in the bile of the ox and other animals, in the form of its sodium salt, $\text{C}_{26}\text{H}_{44}\text{O}_7 \cdot \text{NSNa}$. It crystallises in

¹ *Glycerophosphoric acid*, $\text{C}_3\text{H}_5(\text{OH})_2 \cdot \text{O} \cdot \text{PO}(\text{OH})_2$, is a thick syrup, prepared from glycerol and metaphosphoric acid; salts of glycerophosphoric acid are used in medicine as a source of phosphorus.

needles, is readily soluble in alcohol, and is dextrorotatory. When boiled with alkalis, it gives cholic acid (as a salt) and taurine,



Cholic acid, $\text{C}_{24}\text{H}_{40}\text{O}_5$, crystallises in plates (m.p. 195°), which are sparingly soluble in water, readily so in alcohol and ether; its solutions are dextrorotatory.

In addition to cholic acid, several other closely related acids occur, in combination with glycine or taurine, in the bile of man and of various animals (Part III.).

Taurine, $\text{NH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{SO}_3\text{H}$ (*β -aminoethanesulphonic acid*), was discovered by Gmelin, in 1824, in ox-gall (see p. 564). It is readily soluble in water, but insoluble in alcohol, and decomposes at about 240° ; it is neutral to indicators, but forms salts, such as the sodium salt, $\text{NH}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{SO}_3\text{Na}$, with bases.

Taurine has been prepared by carefully treating alcohol with sulphur trioxide to form *carbyl sulphate*, $\begin{array}{c} \text{CH}_2 - \text{O} - \text{SO}_2 \\ | \qquad \qquad | \\ \text{CH}_2 \cdot \text{SO}_2 \cdot \text{O} \end{array}$, which on hydrolysis gives isæthionic acid, $\text{SO}_3\text{H} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{OH}$. This crystalline acid, with phosphorus pentachloride, yields (the acid chloride of) *chloroethanesulphonic acid*, $\text{CH}_2\text{Cl} \cdot \text{CH}_2 \cdot \text{SO}_3\text{H}$, from which taurine is obtained with the aid of ammonia.

Cholesterol, $\text{C}_{27}\text{H}_{45} \cdot \text{OH}$, is an unsaturated monohydric alcohol which occurs in bile, in the brain, and in considerable quantities (up to 98 per cent.) in certain gall-stones and cancerous and tubercular deposits; it is also found in the yolk of egg and in some vegetable oils; the fat (lanoline) obtained from wool, is a mixture of cholesteryl palmitate, stearate, and oleate.

Cholesterol is readily obtained by extracting common gall-stones with absolute alcohol, boiling the extract with a little potash, and then precipitating the concentrated solution with water; the product is washed with water and crystallised from a mixture of ether and alcohol.

Cholesterol separates from ether in plates, melts at 148° , and distils at about 360° without appreciable decomposition; it is lævorotatory and insoluble in water. In the lower intestine it is reduced to *coprosterol*, $\text{C}_{27}\text{H}_{47} \cdot \text{OH}$.

Reactions of Cholesterol.—When a few centigrams of cholesterol are dissolved in chloroform (2 c.c.) and the solution is shaken with concentrated sulphuric acid (2 c.c.), the chloroform solution is coloured red and then purple, and the sulphuric acid acquires a green fluorescence.

Concentrated sulphuric acid, containing a little iodine, colours cholesterol violet, then blue, then green, and lastly red. Warmed with dilute (20 per cent.) sulphuric acid, cholesterol crystals are coloured red at the edges.

Several other compounds related to cholesterol, and classed as *phytosterols*, have been found in the vegetable kingdom.

Ergosterol, $C_{28}H_{43}\cdot OH$, occurs in ergot and in yeast, and is probably widely diffused in animals and plants; it melts at 154° , and is lævorotatory.

When ergosterol (usually prepared from yeast) is exposed to ultra-violet light, it is partly converted into a resinous or waxy product, which is a mixture of various isomerides of the sterol (produced successively) and from which a crystalline compound, *calciferol*, can be isolated.

Calciferol, $C_{28}H_{43}\cdot OH$, is a vitamin (p. 570), distinguished as vitamin D_2 ; it was the first of these most important compounds to be isolated and is used in medicine on account of its curative action in cases of rickets. It is so potent in this respect that the effect of a daily dose of only 1/400,000 mg. during 14 days can be detected. Since cholesterol and probably other sterols occur in the human skin, the well-known beneficial effects of sunlight in cases of rickets seem to be the result of the production of vitamin D_2 from one or more of the sterols in the animal body.

Stigmasterol, $C_{29}H_{47}\cdot OH$, is also an important phytosterol; it occurs in the soya- and calabar-bean.

All the bile acids and the sterols are related to one another in structure, since they can all be converted into *cholanic acid*, $C_{24}H_{40}O_2$; the framework of the molecule of this compound is a fully reduced phenanthrene complex, which is *condensed* with a closed chain of 5-carbon atoms in the 1:2 position (p. 502).

Hormones.

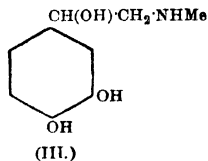
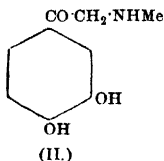
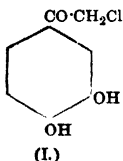
Certain small organs of the body, which at one time seemed to have no particular function, are now known to produce internal secretions, which do not pass to other parts of the body through definite channels, but are absorbed by the veins of the gland into the blood system. The secretions of such ductless or *endocrine* glands contain substances, named **hormones** (*δρμή*, an impulse) by Starling, which are most extraordinarily active, which play a highly important part in exciting or regulating the action of other organs, and the deficiency or excess of which leads to serious or fatal

results. Three of the better-known hormones are described below ; of these, adrenaline and thyroxine, especially the former, are very simple substances, compared with many animal products, their constitutions are known, and they have been synthesised.

***l*-Adrenaline**, $C_9H_{13}O_3N$ (adrenine, epinephrine), is the hormone produced in the very small organs known as the supra-renal or adrenal glands, and was obtained in a crystalline form by Aldrich and by Takamine in 1901. When injected into the blood system, it causes a contraction of the arteries and a very considerable increase in the blood pressure, the effect of a dose of 0.001 mg. given to a cat being recognisable.

Adrenaline is a crystalline, lævorotatory, secondary base (m.p. 216°), sparingly soluble in water, but readily soluble in caustic alkalis ; its phenolic character is shown by its behaviour towards alkalis, and also by the fact that, like catechol (p. 431), it gives an intense green colouration with ferric chloride. It is decomposed by boiling alkalis, giving methylamine ; it affords protocatechuic acid (p. 533) when it is fused with alkalis, and when it is exhaustively methylated and then oxidised, it is converted into trimethylamine and *veratric* acid, $C_6H_3(OMe)_2 \cdot COOH$ [2 OMe = 3:4], a dimethyl-derivative of protocatechuic acid.

From these and other facts the structural formula (III.) was assigned to adrenaline, and was fully established by the following synthesis: Catechol, when it is treated with chloroacetyl chloride, gives chloroacetylcatechol (I.), which, with an excess of methylamine, is converted into a crystalline, substituted ketone, *adrenalone* (II.) ; this compound, reduced with aluminium amalgam and water, gives *dl*-adrenaline (III.) :



The *dl*-base is only about one-half as potent as the *l*-base ; when its hydrogen tartrate is fractionally crystallised from methyl alcohol, the *lBdA* salt separates, and the base, obtained from this salt, is identical in every respect with *l*-adrenaline. The *d*-base, which remains as hydrogen tartrate in the mother liquors, is readily

racemised by hydrochloric acid ; from the *dl*-compound thus formed further quantities of the *l*-base are obtained.

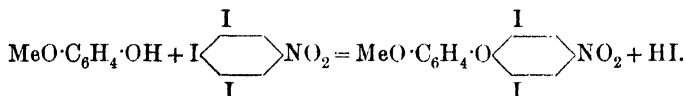
The physiological activity of *d*-adrenaline is only about $\frac{1}{15}$ th of that of the *l*-base.

***l*-Thyroxine**, $C_{15}H_{11}O_4I_4N$, is a hormone which occurs, combined with a protein, in the thyroid gland, the defective development of which was found to be associated with cretinism and myxœdema, whereas its abnormal enlargement was observed in cases of goitre ; preparations of the thyroid glands of animals, administered by the mouth, were found to have a very beneficial effect on patients suffering from cretinism and myxœdema, so that a relation between the gland and these diseases was established. In 1896 Baumann discovered that the thyroid contained combined iodine, and twenty years later a crystalline iodo-compound was isolated from it by Kendall ; minute doses of this compound, which he named *thyroxine*, were found to have the same beneficial effect on the above-mentioned diseases as large quantities of the gland-substance.

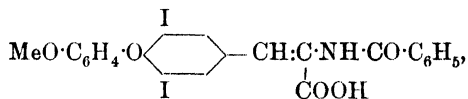
The molecular formula of thyroxine was determined by Harington, who also showed that, on reduction with hydrogen in alkaline solution in the presence of colloidal palladium, the iodine was displaced by hydrogen, giving a primary base, *desiodothyroxine*, $C_{15}H_{15}O_4N$, from which, by exhaustive methylation and decomposition of the quarternary salt, he obtained an unsaturated acid, $MeO \cdot C_6H_4 \cdot O \cdot C_6H_4 \cdot CH:CH \cdot COOH$; on oxidation, this acid gave an aldehyde, $MeO \cdot C_6H_4 \cdot O \cdot C_6H_4 \cdot CHO$, and the corresponding acid. When fused with potash, desiodothyroxine was converted into quinol, *p*-hydroxybenzoic acid, a phenol, $HO \cdot C_6H_4 \cdot O \cdot C_6H_4 \cdot CH_3$, derived from phenyltolyl ether, oxalic acid and ammonia.

The constitutions of these various degradation products of desiodothyroxine having been determined, and collateral evidence as to the positions of the iodine atoms in thyroxine having been obtained, it was possible to assign to the latter the structural formula given later ; this formula was finally established by the following synthesis, accomplished by Harington and Barger, and now used for the commercial preparation of thyroxine :

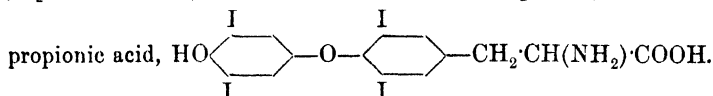
A solution of *p*-methoxyphenol, treated with 3:4:5-triiodonitrobenzene in the presence of anhydrous potassium carbonate, gives a methoxynitrodiiodo-derivative of diphenyl ether,



The nitro-group in this compound is successively transformed into $-\text{NH}_2$, $-\text{N}_2\text{X}$, and $-\text{CN}$ by the usual methods (p. 404), and the cyano-derivative is reduced to the aldimine with anhydrous stannous chloride and hydrogen chloride in ethereal solution (p. 438). The aldehyde obtained from the aldimine, is condensed with hippuric acid, and the product,



is boiled with concentrated hydriodic acid, acetic anhydride, and red phosphorus, by which it is converted into the saturated amino-acid, $\text{HO} \cdot \text{C}_6\text{H}_4 \cdot \text{O} \cdot \text{C}_6\text{H}_2\text{I}_2 \cdot \text{CH}_2 \cdot \text{CH}(\text{NH}_2) \cdot \text{COOH}$, by reduction and displacement of the methyl- and benzoyl-groups by hydrogen. Finally this saturated *dl*-amino-acid is treated with potassium triiodide in ammoniacal solution and is thus converted into β -[3:5-diiodo-4-(3:5-diiodo-4-hydroxyphenoxy)]-phenyl- α -amino



This *dl*-acid, resolved *indirectly*, gave an *l*-acid, identical with thyroxine in physical, chemical, and physiological properties.

Insulin is a hormone, which is secreted by the islet cells (*islets of Langerhans*) of the pancreas of man and of animals, and is of great physiological importance. It has been known for about forty years that the removal of the pancreas brings on the symptoms of *diabetes mellitus*, and it seemed very probable, therefore, that this disease was closely connected with some deficiency in that organ; it was not, however, until 1922 that Banting and Best succeeded in separating from the pancreas a stable preparation which, when injected into the system, was found to diminish the proportion of glucose in the blood, and to produce a wonderful improvement in the condition of patients suffering from diabetes.

'Men declining quickly or slowly through stages of weakness and pain to early death, have been brought within a few days

back to full working powers ; sufferers carried to hospital, actually dying of diabetes, already helpless and unconscious, have been resuscitated as by some magic, and have been brought back almost at once to normal life by help of this remedy.'¹

The preparation, or the hormone contained in it, which produces these effects was named *Insulin* by the discoverers.

A crystalline preparation of insulin, which is lævorotatory, has been described by Abel, who assigns to it the empirical formula, $C_{45}H_{69}O_{14}N_{11}S, 3H_2O$, but little is yet known of its structure ; it is certainly a very complex substance, having a molecular weight of at least 20,000 ; it gives some of the reactions of proteins, and on hydrolysis affords a mixture of many amino-acids.

Vitamins.

The work of many investigators, extending over a very long period, gradually led to the conclusion that normal health depended not only on the quantity of food, which is consumed, and the composition of its main components, but also on some factor or factors quite unknown.

Scurvy, for example, which in days gone by was rife among sailors during long voyages, was prevented to a greater or less extent by the addition of lemon juice to the men's rations. Much later it was found that *beri-beri*, a disease common in the East, was due to a diet of cleaned or polished rice, and could be cured by adding an alcoholic extract of the polishings to the food of the sufferer. From the alcoholic extract of the polishings, there was obtained a highly potent, nitrogenous material which was called '*vitamine*' by Funk, but this preparation was a mixture, and its active component was not isolated.

In 1906, it was shown by Hopkins that although a mixed diet of ordinary food consisting of carbohydrates, fats, proteins, and mineral matter, may be sufficient for normal nutrition, a diet of the same substances, after they have been 'purified,' may be totally inadequate and give rise to various diseases ; he also proved that fresh milk contains something, other than the components just mentioned, which is essential to a growing animal.

It was then found that many other food stuffs, such as butter,

¹ Report of Medical Research Council.

egg-yolk, wheat-germ, orange-juice, fresh vegetables, &c., also contain some very active components which are essential to normal health; these unknown compounds were named *vitamins* and were distinguished as vitamin A, B, &c. according to their effects, or to the results produced by their absence. Later on, it was found that certain active extracts or preparations which had been regarded as *a* vitamin, were mixtures of active substances, each of which had a specific physiological effect; these components, of vitamin B for example, were then distinguished as B₁, B₂, and so on.

Vitamin A enables an organ to resist infection and restores the growth of young animals suffering from a diet deficient in this vitamin; it does not itself occur in food, but is produced in the body from *carotene* (Part III.) which is found in many plants, such as carrots, spinach, tomatoes, &c., and also in cod-liver oil.

When about 0.1 g. of an oil or fat, dissolved in chloroform, is added to about 2 c.c. of a 30 per cent. solution of antimony trichloride, a blue colouration is obtained, owing to the presence of vitamin A.

Vitamin B (a mixture of B₁, B₂, &c.) is present in rice-polishings, yeast, liver, and many vegetables; its absence from a diet brings on *beri-beri* and retarded growth. Vitamin C is contained in many vegetables and in lemon-juice, which has long been used as an antiscorbutic or preventive of scurvy. It is a crystalline, optically active compound, C₆H₈O₆, and is also called *ascorbic acid* (Part III.). Vitamin D₂ (calciferol, p. 566) is concerned with the calcification of bones and teeth; its absence causes rickets. It occurs in cod-liver oil, which was used in medicine as a cure for rickets long before vitamins were discovered, and also in the oil from halibut- and other fish-livers. The discovery of its formation from ergosterol was of very great importance, and its almost incredible potency is indicated by the statement already made (p. 566). Vitamin E is contained in large proportions in wheat-germ and its absence brings about sterility. All vitamins seem to originate in the vegetable kingdom, those present in animal products (eggs, butter, cod-liver oil, &c.) having been produced in the body from vegetable food.

Vitamins may be compared with hormones and with enzymes, since a minute quantity of any member of any of these groups is capable of bringing about within the body chemical changes, which are essential to normal life.

The wonderful success which has already crowned the efforts of chemists and biologists in the investigation of the hormones and the vitamins is of outstanding importance for the welfare of mankind. When the difficulties of separating a vitamin of unknown properties, from relatively enormous masses of animal or vegetable matter, were considered, it seemed that the task was well-nigh impossible, and that many years must elapse before even the most abundant of these substances could be isolated. In fact, however, to some extent owing to chance discoveries, progress has been astonishingly rapid; some of the vitamins have not only been obtained in a state of purity, but their structures have also been determined, and their synthesis accomplished.

The Proteins.

The white of egg, when separated from the yolk, membrane, and shell, is a thick, colourless, transparent, sticky fluid, miscible with water; on exposure to the air it rapidly loses water, and if dried artificially it quickly shrivels up, giving 12–15 per cent. of a translucent amorphous solid, which contains some mineral matter.

When white of egg is put into boiling water it undergoes a remarkable change, and is said to have *coagulated*; it is now insoluble in water and opaque, and forms a solid mass, which, however, still contains a large percentage of water; during coagulation, it is probable that chemical as well as physical changes have occurred.

When white of egg is left exposed to the air under ordinary (non-sterile) conditions it soon begins to putrefy—that is to say, it decomposes owing to the action of organisms, yielding a great number of products, among which are hydrogen sulphide, ammonia, ptomaines (p. 545), and various amino-acids (p. 542). Further, when white of egg is heated with dilute mineral acids or with alkalis, it undergoes a profound decomposition, giving in the first place various highly complex products (albumoses, pro-peptones, peptones), and finally a large number of simpler compounds, of which the amino-acids are the most important. Similar results are obtained with the aid of digestive enzymes, such as pepsin.

This brief account of the behaviour of white of egg will suffice to show that it is an extremely unstable and extraordinarily complex substance. When its aqueous solution is half-saturated with ammonium sulphate, a part of it (egg-globulin) is precipitated and a part (egg-albumin) remains in solution, but both these products are probably mixtures; the globulin differs from the albumin, inasmuch as it is not soluble in water, except in the presence of a certain very small proportion of mineral salts, but otherwise there is little known difference between the two products.

Now egg-albumin and egg-globulin may be taken as representatives of a very ill-defined group of substances, which are classed together as the **proteins**. Such substances form not only the most important part of the contents of the cells of all animals (*πρωτεϊον*, pre-eminence), but they also occur in considerable quantities in all plants, especially in the seeds (peas, beans, cereals, &c.); it is, in fact, from these vegetable proteins that those contained in animals are formed, since the animal, unlike the plant, is incapable of building up its tissues from carbon dioxide, water, and mineral matter. The vegetable proteins, then, are assimilated by animals, and apparently they are changed very little during this process.

The proteins are all *polypeptides* (p. 546), and in the complex chain each amino-acid residue occurs, apparently, at regular intervals. They differ very considerably in physical properties, but the following general statements may be made: The proteins are insoluble in alcohol and ether, and also, as a rule, in water; but many of them dissolve in salt solutions, and the presence of salts accounts for the solubility of the proteins in the fluids of the animal body. They are all optically active (*lævorotatory*), and most of them are colloids. One of the more interesting properties shown by some of the proteins is that of undergoing *coagulation* (p. 572), a change which is readily brought about by heat; but different proteins coagulate at somewhat different temperatures, varying roughly between 55° and 75°, and some are also coagulated by alcohol and by mineral acids.

All proteins consist of carbon, hydrogen, oxygen, nitrogen, and sulphur, and some contain phosphorus as well, but the determination of the percentage composition of a protein is a very difficult task. As found in nature, all proteins contain

mineral matter, and consequently, on ignition, leave a small percentage of ash; after the removal of these mineral components by repeated precipitation, dialysis, &c., or when their presence is allowed for, the percentage composition of the various proteins is found to vary within fairly wide limits, as shown by the following numbers:

Carbon	50.0–55.0 per cent
Hydrogen	6.9– 7.3 "
Nitrogen	15.0–19.0 "
Oxygen	19.0–24.0 "
Sulphur	0.3– 2.4 "

Egg-albumin has been obtained free from mineral matter by dialysis and in a crystalline condition; its composition is C = 51.48, H = 6.76, N = 18.14, O = 22.66, S = 0.96 per cent.

The *empirical* formula, calculated from the percentage composition of egg-albumin, or from that of some other protein, comes out to something like $C_{146}H_{226}O_{50}N_{44}S$, which requires C = 51.2, H = 6.6, N = 18.0, and S = 0.9 per cent.; as, however, a very slight error in the analytical results would make a very great difference in the empirical formula, that just given is only a rough approximation.

The molecular weights of some of the proteins have been determined by various methods, and from the concordant experimental results, it may now be inferred with some assurance, that the minimum value for the simpler proteins is at least 17,000, which is about fourteen times as great as that of the octadecapeptide synthesised by E. Fischer (p. 547). The molecular weights of the more complex substances are certainly very much higher than 17,000, and some of them, it would seem, even exceed several millions.

The proteins are classed into various groups, principally according to their physical properties. Those which are coagulated by heat (in the presence of mineral salts), for example, may be classed as (a) albumins or (b) globulins. The *albumins* (egg-albumin, blood-albumin) are soluble in water, and are not precipitated when their solutions are saturated with sodium chloride or magnesium sulphate. The *globulins* (serum-globulin) are insoluble in water, but dissolve in dilute salt solutions, from which

they are precipitated when the solutions are saturated with magnesium sulphate.

The *phospho-proteins* (caseinogen, p. 576) contain phosphorus and have an acidic character, in consequence of which they dissolve in alkalis, giving solutions which do not coagulate when they are heated.

Many other classes of proteins are distinguished.

Closely related to the proteins are the complex degradation products (*albumoses, propeptones, peptones, and polypeptides*) which are successively formed when proteins are hydrolysed with the aid of digestive enzymes (pepsin, trypsin, &c.) or chemical reagents; the final products of hydrolysis, as already stated, are complex mixtures of various amino-acids (p. 543).

Tests for Proteins.—All proteins are coloured red by a hot solution of mercuric nitrate containing traces of nitrous acid. This reagent (*Millon's reagent*) is prepared by dissolving one part by weight of mercury in two parts of strong nitric acid and diluting the solution with twice its volume of water; after some time the supernatant liquid is decanted.

When a protein is warmed with nitric acid, it gives a yellow colour, which becomes bright-orange on the addition of ammonia. This reaction (*xanthoproteic reaction*) is stated to be the most delicate test for proteins. When an excess of potash is added to a protein, and then a few drops of copper sulphate solution, a red to violet colouration is produced; this test is called the *biuret reaction*, because it resembles the colour-reaction obtained in a similar manner with biuret (p. 240).

When a protein, or one of its degradation products (see above), is warmed with an aqueous solution of triketohydrindene hydrate (ninhydrin, p. 491), it gives a deep-blue colouration (compare amino-acids, p. 544).

Hæmoglobin is the name given to the protein which constitutes the pigment of the red blood-corpuscles. 'It exists in the blood in two conditions; in arterial blood, it is loosely combined with oxygen, and is called *oxyhæmoglobin*; the other condition is the deoxygenated or reduced hæmoglobin (often simply called *hæmoglobin*), which occurs in venous blood—that is, the blood which is returning to the heart, after it has supplied the tissues with oxygen. Hæmoglobin is thus the oxygen-carrier of the body, and it may be called a respiratory pigment.'¹

Oxyhæmoglobin can be obtained by mixing defibrinated blood with

¹Halliburton, *Chemical Physiology*.

salt solution (1 vol. of saturated salt solution to 9 vols. of water), which precipitates the blood-corpuscles. These are washed with salt water of the same strength, mixed with a little water, and extracted with ether, which removes cholesterol, &c., all these operations being conducted as nearly as possible at 0°. The aqueous solution is then filtered, and the filtrate is mixed with one-fourth of its volume of alcohol, and cooled to -10° ; the crystals of oxyhæmoglobin which separate may be purified by recrystallisation from ice-cold aqueous alcohol.

Oxyhæmoglobin forms light-red rhombic prisms, which dissolve readily in water and are reprecipitated by alcohol. Its percentage composition is nearly the same as that of egg-albumin (p. 574), except that oxyhæmoglobin always contains 0.33 per cent. of iron; on the assumption that one molecule of hæmoglobin contains one atom of iron, the calculated molecular weight would be about 17,000, but there is evidence that this value is far too low. When oxyhæmoglobin, in aqueous solution, is placed under greatly reduced pressure, or treated with weak reducing agents, it loses oxygen and is converted into *hæmoglobin*, a substance which has also been obtained in a crystalline form; on the other hand, hæmoglobin, in aqueous solution, is rapidly converted into oxyhæmoglobin in contact with the air. When carbon monoxide is led into a solution of oxyhæmoglobin, the last-named substance loses its oxygen and combines with the carbon monoxide to form *carbonic oxide hæmoglobin*, a compound which forms bluish-red crystals. This compound is not capable of absorbing and giving up oxygen as is hæmoglobin—a fact which explains the very poisonous action of carbon monoxide. Oxyhæmoglobin, hæmoglobin, and carbonic oxide hæmoglobin all show characteristic absorption spectra, which allow of their being easily identified and distinguished from one another.

Hæmin and Hæmatein.—When oxyhæmoglobin or dried blood is heated with a drop of acetic acid and a small crystal of common salt on a microscopic slide, it is decomposed into a protein and *hæmin*, $C_{33}H_{32}O_4N_4FeCl$, the chloride of hæmatein, which separates in reddish-brown crystals, when the mixture is cooled. When these crystals are treated with alkali, brownish-red flocks of *hæmatein*, $C_{33}H_{32}O_4N_4Fe\cdot OH$, separate; and this formation of hæmin and hæmatein serves as a very delicate test for blood.

Caseinogen (*casein*) is an important protein, which is contained in milk, probably in the form of a soluble calcium salt. When

milk turns sour, as the result of lactic fermentation (p. 157), or is treated with an acid, the calcium salt is decomposed and impure caseinogen is precipitated as a curd, together with some of the fat, while the milk-sugar (lactose) remains in the aqueous solution (whey). The caseinogen may be purified by dissolving it in very dilute alkali and reprecipitating it with very dilute acetic acid.

Rennet, an aqueous extract prepared from the stomach of the calf, also has the property of curdling milk, and is used for this purpose in the manufacture of cheese.

The curd in this case is different from that obtained with acids and is regarded as the insoluble calcium salt of a decomposition product of caseinogen, called *casein*, which is produced from caseinogen, in the presence of calcium salts, by an enzyme, *rennin*, contained in the rennet.

Caseinogen has an acidic character and dissolves in dilute alkalis; it contains about 0.85 per cent. of phosphorus, but otherwise resembles albumin and other proteins in composition. On hydrolysis casein gives all the amino-acids previously described, and its molecule must be of great complexity.

Chlorophyll is the green colouring matter of plants; it may be extracted from dried leaves with the aid of 90 per cent. aqueous alcohol, and thus obtained as a green, amorphous mass. This product is a mixture of two nearly related compounds, distinguished as chlorophyll *a*, $C_{55}H_{72}O_5N_4Mg$, and chlorophyll *b*, $C_{55}H_{70}O_6N_4Mg$, respectively; it is noteworthy that magnesium is an essential constituent of these substances. Very considerable progress has been made in the determination of the structures of the chlorophylls, largely as the result of Willstätter's work, and it is known that both hæmoglobin and chlorophyll give pyrrole derivatives (p. 521) as degradation products.

Chlorophyll, like hæmoglobin, shows a characteristic absorption spectrum, and the absorption spectra and other properties of certain chlorophyll derivatives are almost identical with those of certain derivatives of hæmoglobin. As the function of hæmoglobin is to absorb oxygen, that of chlorophyll to set free oxygen from carbonic acid, this close relationship between the two compounds is of great physiological interest.

Gelatin is a substance closely related to the proteins; it may

be obtained by the action of dilute acids on the protein, *collagen*, which is contained in white fibrous connective tissue.

It may be prepared by digesting bones, first with dilute acids to remove inorganic matter, and then with water under pressure at 110–120°; when the filtered solution is evaporated, commercial gelatin is obtained.

Gelatin is a hard, almost transparent, horn-like substance, which is insoluble in alcohol, ether, and in cold water, but dissolves readily in hot water, yielding a solution which sets to a jelly (*gelatinises*) as it cools. When, however, the aqueous solution is boiled during some hours, the property of gelatinising is entirely lost. Gelatin forms an insoluble compound with tannic acid, and the process of tanning consists partly in converting the gelatin in the hides into this hard, insoluble compound, by steeping them in tannic acid solution. Gelatin is also rendered insoluble in water when it is treated with formaldehyde. When heated with dilute sulphuric acid, gelatin breaks down, much in the same way as do the proteins, yielding glycine, hydroxyproline, proline, alanine, leucine, and many other amino-acids.

CHAPTER XL.

DYES AND THEIR APPLICATION.

ALTHOUGH most organic compounds are colourless, some, especially certain classes of the aromatic series, are intensely coloured substances, amongst which representatives of almost every shade occur; nearly all the principal dyes used at the present day, in fact, are aromatic compounds, the primary source of which is coal-tar—hence the well-known expression ‘coal-tar colours.’ The first of such dyes, *mauve* or *mauveine*, discovered by Perkin (in 1856) was obtained by the oxidation of crude aniline; for this reason those subsequently prepared from other coal-tar components were also called ‘aniline dyes.’

That a dye must give rise to colour is, of course, obvious, but a coloured substance is not necessarily a dye, in the ordinary sense of the word, unless it is also capable of fixing itself, or of being fixed, on the fabric to be dyed, in such a way that the colour is

not removed when the fabric is rubbed, or washed with water; azobenzene (p. 410), for example, is coloured, but it would not be spoken of as a dye, because it does not fulfil the second condition.

Again, when a piece of *silk* or *wool* is soaked in a solution of picric acid, it is dyed yellow, and the colour is retained when the material is washed with water. When, however, a piece of *calico* or other *cotton* material is treated in the same way, the picric acid is dissolved out again by the water and the fabric is not dyed. A given substance, therefore, may be a dye for certain materials, but not for others; silk and wool are dyed by picric acid, but cotton is not—a behaviour which is repeatedly met with in the case of other colouring matters.

Now, materials such as wool, cotton, silk, rayon, &c., consist of minute hollow or solid fibres, the walls of which, like parchment paper and certain membranes, allow of the passage of water and of dissolved crystalloids by diffusion, but not that of colloid substances, or, of course, of matter in coarse suspension. If, therefore, picric acid were present in a fibre, as picric acid, it should be extracted from this fibre by water; since, in the case of silk and wool, this does not occur, it may be assumed that the picric acid has actually combined with some substance in the fibre, and has thus been converted into a yellow compound, which is insoluble in water.

The nature of the insoluble products which are thus formed when a material is dyed, is not known, but there are reasons for supposing that certain components of the fibre unite with the dye to form an insoluble salt. This seems probable from the fact that nearly all dyes, which thus fix themselves directly on the fabric, are either basic, acidic, or amphoteric in character. Azobenzene, as already mentioned, is not a dye, probably because it is a neutral substance; if, however, some group, such as an amino-, alkylamino-, or hydroxyl-group, which possesses basic or acidic properties, is introduced into the molecule of azobenzene, then the resulting derivative is a dye, probably because it has the property of combining directly with the components of certain fibres.

Another fact which leads to the same conclusion may be given. Certain dyes—as, for example, rosaniline—are salts of bases, which are themselves colourless, and yet some materials may be dyed

simply by immersion in the *colourless* solutions of these bases, the same colour being obtained as with the coloured salt (that is, the dye itself); this can be easily explained on the assumption that some component of the fibre combines with the colourless base, forming with it a salt of the same colour as the dye. Some fibres, especially those of silk and wool, seem to contain both acidic and basic components, as they are often dyed directly both by basic and by acidic dyes; cotton (cellulose), on the other hand, which is free from salt-forming components, does not combine with either type of dye except in rare cases.

In spite of facts such as these, the chemical theory of dyeing does not account for the phenomena in all cases.

Since the fixing of a dye within the fibre is probably the result of the conversion of the dye into some insoluble compound, it seems reasonable to suppose that, even if a colouring matter does not combine with any component of the fibre, it might still be employed as a dye, provided that, after it had once passed into the substance of the fibre, it could be there converted into some insoluble product; this principle is applied in the case of many dyes, and the compounds used to fix them in the fibre are termed *mordants*.

Dyes, therefore, may be roughly divided into two classes with respect to their behaviour towards a *given* fabric: (a) *Direct* or *substantive* dyes, which fix themselves on the fabric, and (b) *Indirect* or *adjective* dyes, which do so only with the aid of a mordant. These terms are merely relative; a dye may be *direct* with respect to wool and silk, *indirect* with respect to cotton, a general behaviour, illustrated above (p. 579) in the case of picric acid.

Mordants are substances which (usually after having undergone some preliminary change) combine with dyes, forming insoluble coloured compounds; the colour of the dyed fabric, in such cases, depends on that of the compound thus produced, and not on that of the dye itself, so that by using different mordants, different shades or colours are often obtained.

As an example of dyes of the second class, alizarin may be taken, as its applications illustrate very clearly the use of mordants.

When a piece of calico is soaked in an aqueous solution of

alizarin, it is coloured *yellow*, but the colour is not fixed, and is easily removed with the aid of soap and water. When, however, a piece of calico, which has been previously mordanted with a suitable aluminium salt (in the manner described below), is treated in the same way, it is dyed a fast *red*, the alizarin having combined with aluminium hydroxide in the fibre to form a red insoluble substance; if the calico had been mordanted with a ferric salt, it would have been dyed a fast *dark violet*.

A substance such as alizarin, which can thus be used for the production of different colours, is termed a *polygenetic* dye; one which gives one colour only, is a *monogenetic* dye.

Compounds very frequently employed as mordants are certain inorganic salts of iron, aluminium, chromium (alums), and tin, and also organic salts, such as the acetates and thiocyanates, from which an insoluble metallic hydroxide or basic salt can be easily obtained by hydrolysis with water.

The process of mordanting cotton involves two operations: firstly, the fabric is passed through, or soaked in, a solution of the mordant, in order that its fibres may become impregnated with the metallic salt; secondly, the fabric is treated in such a way that the salt is decomposed within the fibres, and there converted into some insoluble compound.

The second operation, the fixing of the mordant, so that it will not be washed out when the fabric is brought into the dye-bath, is accomplished in many ways. One method is to pass the mordanted material through a solution of some weak alkali (ammonia, sodium carbonate, lime), or of some salt, such as sodium phosphate or arsenate, which reacts with the metallic salt in the fibre, forming an insoluble metallic hydroxide, or a phosphate, arsenate, &c. Another method, applicable in the case of mordants which are salts of *volatile acids*, consists in exposing the treated fabric to the action of steam, at a suitable temperature; under these conditions the metallic salt is hydrolysed, the acid volatilises with the steam, and an insoluble hydroxide or basic salt remains in the fibre (compare p. 153).

In the case of silk and woollen fabrics, the operations of mordanting and fixing the mordant are commonly carried out simultaneously, by merely soaking the materials in a boiling dilute solution of the mordant; under these conditions the metallic salt

is hydrolysed in the fibre, and the product is there retained in an insoluble form; silk is sometimes merely soaked in a cold, concentrated solution of the mordant, and then washed with water to cause the hydrolysis of the metallic salt.

In cases where only parts of the fabric are to be dyed, as, for example, in *calico-printing*, a solution of a suitable mordant may be mixed with the dye, and with some thickening substance, such as starch, dextrin, gum, &c., and printed on the fabric in the required manner, the thickening being used to prevent the mordant and dye from spreading to other parts; the material is then submitted to a steaming process, when the metallic hydroxide, which is produced within the fibre, combines with and fixes the dye.

All these processes are identical in principle, the object being to deposit within the fibre some insoluble compound, which, when afterwards treated with a solution of a suitable dye, forms a coloured substance, stable in the light and towards soap and water. The coloured substances produced by the combination of a dye with a metallic hydroxide are termed *lakes*, and those dyes which form lakes belong to the class of *acid* dyes.

Tannin (p. 473) is an example of a different class of mordants—namely, of those which are employed with *basic dyes*, such as malachite green (p. 585) and rosaniline (p. 588). The fabric is mordanted by being passed first through a solution of tannin, and then through a weak solution of tartar emetic, or stannic chloride; the tannin is thus converted into an insoluble antimony or tin tannate, which converts the basic dye into an insoluble colloidal product, and thus fixes it in the fibres.

Many organic dye-stuffs are transformed into colourless compounds on reduction, and when the reduction product can be reconverted into the dye by oxidation, it is called a *leuco-compound*.

When an insoluble dye yields a *soluble* leuco-compound, which is very readily reconverted into the dye on oxidation, it may be applied to fabrics in a special manner, as, for example, in the case of indigo-blue. Indigo-blue, $C_{16}H_{10}O_2N_2$ (p. 606), is insoluble in water, but on reduction it is converted into a leuco-compound, $C_{16}H_{12}O_2N_2$, known as *indigo-white*, which is soluble in aqueous alkalis. In dyeing with indigo, an alkaline solution

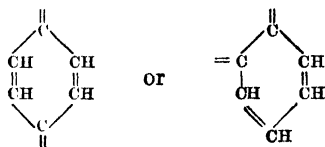
of indigo-white is prepared by reducing indigo, suspended in water, with a suitable reagent, and the fabric is then passed through this solution, whereon the indigo-white diffuses into the fibres through their walls; on subsequent exposure to the air, the indigo-white is reconverted into indigo-blue by oxidation, and the insoluble dye is thus fixed in the fabric.

This is an example of the process of *vat-dyeing*, which has the very great advantage of not requiring any mordant. Another method of dyeing, of increasing importance, applicable in the case of azo-dyes, is the direct formation of an insoluble dye-stuff within the fibres, by the process of coupling, as described later (p. 599). In both these processes, since the dye-stuff is produced within the fibres, the presence of a particular basic or acidic group (p. 579) is unnecessary; further, the coloured product may be a direct dye to all fibres.

The molecules of nearly all intensely coloured substances contain at least one group of atoms, called a *chromophore*, to the presence of which the colour may be attributed. Thus, in the case of azobenzene, the chromophore is the azo-group, $-N:N-$; a change in this part of the molecule, such as that which occurs when azobenzene is converted into hydrazobenzene, destroys the colour, whereas a change in other parts of the molecule, such as the substitution of various groups for hydrogen atoms of the nucleus, merely modifies the colour.

With few exceptions all hydrocarbons, and all aliphatic compounds, composed of carbon, hydrogen, and oxygen only, are colourless, whereas certain relatively simple aromatic compounds, namely, the *quinones*, which also consist of these three elements, are distinctly coloured, but are converted into colourless dihydroxy-derivatives on reduction. These facts seem to show that the colour of quinones is determined by the presence in their molecules of carbonyl groups, $>CO$, associated with ethylenic linkages (compare p. 446), an arrangement which is summarised as a 'quinonoid structure'; the chromophore in such quinones, therefore, is a particular type of di-olefinic closed-chain, in which two of the carbon atoms in the *o*- or *p*-position to one another are united to oxygen by two of their valencies. Molecules derived from the same type of closed-chain, but containing groups such as $>C=NH_2Cl$, $>C=NHMeCl$, $>C=NMe_2Cl$, in the place of one,

or of both, the carbonyl-radicals, are also classed as 'quinonoid,' and are nearly always highly coloured. That this particular type of structure, represented by one of the following symbols,



is the cause of colour in a large number of aromatic compounds, which do not contain the azo-chromophore, was suggested by Armstrong; as a result of this suggestion, it was found that constitutional formulæ, which had been assigned to certain dye-stuffs, and which did not contain any recognised chromophore, could be changed into quinonoid structures, and thus brought into line with those of the simple quinones. Various examples of the application of the quinonoid theory are given later; an apparently simple reaction, such as the loss of a molecule of water or of halogen acid, which brings about the transformation of a colourless into a highly coloured compound, is interpreted as resulting in a complex change of structure, analogous to that by which quinol is converted into quinone (p. 447).

A substance which contains a chromophore is called a *chromogen*, and a group which increases the intensity of the colour and is necessary, in many cases, to render an inert chromogen capable of being used as a dye, is called an *auxochrome*. The amino-, alkylamino-, dialkylamino-, and hydroxyl-groups are the more important auxochromes.

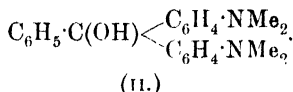
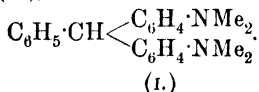
A few typical dyes are described in the following pages; so many of these compounds are known that even important groups have been omitted, partly because of the complexity of their members, but principally because their description would not illustrate any new principle.

Derivatives of Triphenylmethane.

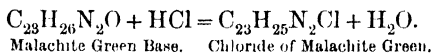
Triphenylmethane, $\text{C}_6\text{H}_5\cdot\text{CH}(\text{C}_6\text{H}_5)_2$ (p. 370), is the parent hydrocarbon, from which various brilliant basic dyes, such as *malachite green*, *pararosaniline*, and *rosaniline* are obtained.

The *leuco-base* (p. 582), in all cases, is a *p*-amino-derivative of triphenylmethane; that of malachite green, for example, is *tetra-*

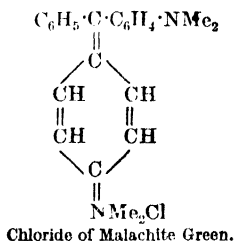
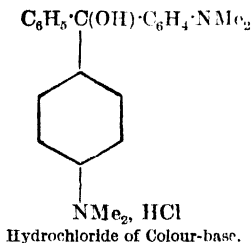
methyl-p-diaminotriphenylmethane (I.), which, on oxidation, is converted into the colour-base, *tetramethyl-p-diaminotriphenyl carb-inol* (II.),



Both the leuco-base and the colour-base are *colourless*, and the latter also yields colourless, or only slightly coloured, salts, on treatment with *cold* acids; when *warmed* with acids, however, the colour-base gives highly coloured salts, which constitute the dye, the elements of water being eliminated,

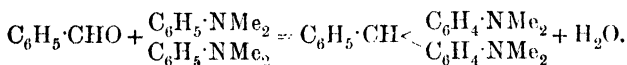


This conversion of the colourless into the coloured salt may be regarded as a complex change, analogous to that by which colourless quinol is transformed into highly coloured quinone (p. 447), and may be represented in the following manner:



Exactly similar changes may be assumed to take place in the formation of the pararosaniline and rosaniline dyes, which may also be represented by quinonoid structures (p. 587).

Malachite green is manufactured by heating a mixture of benzaldehyde (1 mol.) and dimethylaniline (2 mols.) with hydrochloric acid,



The colourless, crystalline leuco-base, tetramethyl-*p*-diaminotriphenylmethane, when treated with lead dioxide and hydrochloric acid, is oxidised to the (colourless) colour-base, tetramethyldi-

aminotriphenyl carbinol, which is converted into the dye by boiling it with an acid, such as oxalic acid. Commercial malachite green is (usually) the oxalate, $2C_{23}H_{24}N_2 \cdot 3C_2H_2O_4$, which forms deep-green crystals, and is readily soluble in water.

Malachite green dyes silk and wool directly an intense dark-bluish green, but cotton must first be mordanted with tannin and tartar emetic (p. 582), and then dyed in a bath gradually raised to 60° .

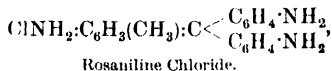
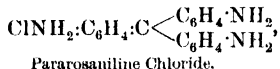
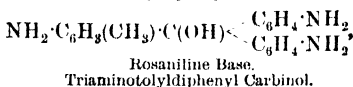
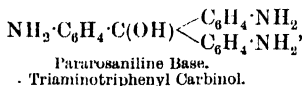
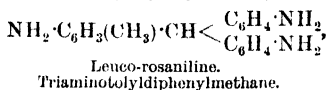
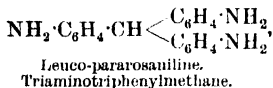
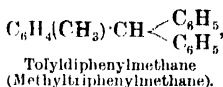
Laboratory Preparation of Malachite Green.—Dimethylaniline (10 parts) and benzaldehyde (4 parts) are heated with finely powdered, *anhydrous* zinc chloride (8 parts) in a porcelain basin on a water-bath, during 4 hours, the mixture being frequently stirred. The product is submitted to distillation in steam, to get rid of the unchanged dimethylaniline, and the insoluble leuco-compound is then washed with water, dissolved in the minimum quantity of boiling alcohol, and the filtered solution left to crystallise over night. The deposit, mixed with further quantities of leuco-base, obtained by concentrating the filtrate, is washed with a little alcohol and dried.

The leuco-base (10 g.) is dissolved in concentrated hydrochloric acid (14 c.c.) and water (900 c.c.), with the addition of glacial acetic acid (4 c.c.), and a paste of the theoretical quantity of finely divided lead peroxide¹ with about 5 parts of water is rapidly stirred into the solution, cooled to 0° . A few minutes later the lead is precipitated with a solution of sodium sulphate, and the filtered liquid is treated with a concentrated solution of zinc chloride (10 g.) and finally with a saturated solution of sodium chloride, until the precipitation of the zinc double salt, $3C_{23}H_{26}N_2Cl \cdot 2ZnCl_2 \cdot 2H_2O$, is practically complete.

Many dyes, closely allied to malachite green, are prepared by condensing benzaldehyde with other tertiary alkylanilines (p. 395). *Brilliant green*, for example, is finally obtained when diethylaniline is employed, instead of dimethylaniline, in the above-described process, whereas *Acid green* is obtained from benzaldehyde and ethylbenzylaniline. Blue dyes are obtained by substituting sulphonic- and hydroxy-radicals for hydrogen atoms of the phenyl-group in Brilliant green, whereas by displacing the phenyl-group by sulphonated naphthalene nuclei, important green dyes, such as *Naphthalene green V*, are produced.

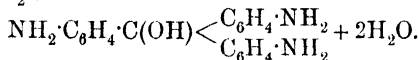
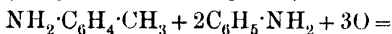
Pararosaniline and *rosaniline* are important dyes, which, like malachite green, are derived from triphenylmethane. Whereas, however, malachite green is a derivative of *diamino*-triphenylmethane, the rosanilines are all *tri-amino*-triphenylmethane derivatives, as will be seen from the following formulæ :

¹ The quality of the lead peroxide is important and should be determined beforehand.

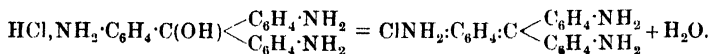


In all these compounds the amino-groups are in the *para*-positions to the methane carbon atom.

Pararosaniline is derived from *triaminotriphenyl carbinol*, a base which is prepared by oxidising a mixture of *p*-toluidine (1 mol.) and aniline (2 mols.) with arsenic acid, or nitrobenzene (compare rosaniline, p. 588),



Probably the *p*-toluidine is first oxidised to *p*-aminobenzaldehyde, $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CHO}$, which then condenses with the aniline (as in the case of the formation of leuco-malachite green) to form leuco-pararosaniline; this compound is then oxidised to the pararosaniline colour-base, triaminotriphenyl carbinol, which is converted into the quinonoid dye by warming it with acids (compare malachite green, p. 585),

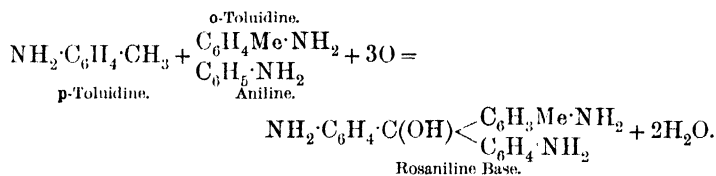


The salts of pararosaniline have a deep-magenta colour, and are soluble in warm water; they dye silk, wool, and cotton under the same conditions as described in the case of malachite green; pararosaniline, however, is not so largely used as rosaniline.

Constitution of Pararosaniline.—Triphenylmethane, with the aid of fuming nitric acid, is converted into *trinitrotriphenylmethane*, $\text{NO}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CH}(\text{C}_6\text{H}_4 \cdot \text{NO}_2)_2$, a compound in which all the nitro-groups are in the *p*-positions to the methane carbon atom; this nitro-compound, on reduction, yields leuco-pararosaniline, which,

on oxidation, is readily converted into the colour-base, triamino-triphenyl carbinol.

Rosaniline, fuchsine, or magenta, is a methyl-substitution product of pararosaniline, and the colour-base is produced by the oxidation of equal molecular proportions of aniline, *o*-toluidine, and *p*-toluidine (with nitrobenzene, arsenic acid, &c.), the reaction being similar in all respects to the formation of the pararosaniline base from aniline (2 mols.) and *p*-toluidine (1 mol.),



To the requisite mixture of aniline, *o*-toluidine, and *p*-toluidine (38 parts), hydrochloric acid (20 parts), and nitrobenzene (20 parts) are added, and the whole is gradually heated to 190°, small quantities (2 per cent.) of iron-filings being added from time to time (see below). At the end of about 8 hours the reaction is complete, and the powdered product is extracted with boiling water, under pressure; lastly, the filtered extract is mixed with salt, and the crude fuchsine, which separates, is purified by recrystallisation.

In this reaction the nitrobenzene acts only indirectly as the oxidising agent; the ferrous chloride, produced by the action of the hydrochloric acid on the iron, is oxidised by the nitrobenzene to ferric chloride, which in its turn oxidises the mixture of aniline and toluidines to rosaniline, and is itself again reduced to ferrous chloride; the action, therefore, is continuous, and only a small quantity of iron is necessary.

The salts of the rosaniline base with one equivalent of an acid, as, for example, the chloride, $\text{C}_{20}\text{H}_{20}\text{N}_3\text{Cl} \cdot 4\text{H}_2\text{O}$, form magnificent crystals, which show an intense green metallic lustre; they dissolve in warm water, forming deep-red solutions, and dye silk, wool, and cotton a brilliant magenta colour, the conditions of dyeing being the same as in the case of malachite green. These salts may be represented by quinonoid structures, as in the case of pararosaniline (p. 587).

Derivatives of Pararosaniline and Rosaniline.

The hydrogen atoms of the three amino-groups in pararosaniline and rosaniline may be displaced by alkyl-groups, by

methods analogous to those used in the manufacture of the alkyl-anilines (p. 395); alkyl- and aryl-derivatives of the two dyes may also be obtained in other ways (below).

The substitution of methyl-groups for hydrogen in the molecule of rosaniline, which is a brilliant red dye, brings about a change in colour—first to reddish-violet, and then to bluish-violet, as the number of alkyl-groups increases. This change is more marked when ethyl-groups are introduced, and still more so when benzyl- or phenyl-radicals are substituted for hydrogen; in the latter case, pure blue dyes are produced (see p. 590). In fact, by varying the number and character of the substituents, almost any shade from red to blue can be obtained.

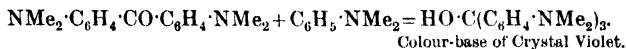
Methyl violet appears to consist principally of the chloride of *pentamethyl-pararosaniline*.

It is manufactured in very large quantities by warming dimethylaniline with copper sulphate, sodium chloride, phenol, and a little water during 6-8 hours; atmospheric oxidation occurs and formaldehyde is evolved, but little is known of the other reactions which take place. The powdered product is extracted with, and then dissolved in, hydrochloric acid, and cautiously treated with sodium sulphide to precipitate copper; the filtered solution is finally evaporated to dryness.

It is readily soluble in alcohol and hot water, forming beautiful violet solutions, which dye silk, wool, and cotton under the same conditions as are employed in the case of malachite green (p. 586). It is extensively used in the manufacture of copying inks, ribbons for type-writers, pencils, &c

Crystal violet is the chloride of *hexamethyl-pararosaniline*, and is manufactured by heating dimethylaniline with carbonyl chloride (phosgene) in the presence of anhydrous zinc chloride.

Tetramethyldiaminobenzophenone (Michler's ketone) is first formed, and then condenses with dimethylaniline, in the presence of zinc chloride, giving the colour base of crystal violet,



Its applications and properties are similar to those of methyl violet.

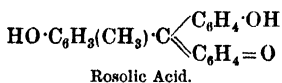
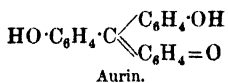
When rosaniline is heated with aniline, in the presence of some acid, such as acetic, benzoic, or oxalic acid, phenyl-groups displace the hydrogen atoms of the amino-groups just as in the formation

of diphenylamine from aniline and aniline hydrochloride (p. 398). Here, as in the case of the alkyl-derivatives of rosaniline, the colour of the product depends on how many phenyl-groups have been introduced into the molecule; the mono- and di-phenyl-derivatives are reddish-violet and bluish-violet respectively, whereas the triphenyl-compound is a pure blue dye, known as *Aniline blue*.

Aniline blue, $\text{C}_6\text{H}_5\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{C}\begin{smallmatrix} \nearrow \text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{C}_6\text{H}_5 \\ \searrow \text{C}_6\text{H}_3(\text{CH}_3):\text{NH}(\text{C}_6\text{H}_5)\text{Cl} \end{smallmatrix}$ (triphenylrosaniline chloride), is very sparingly soluble in water, and in dyeing with it, the operation has to be conducted in alcoholic solution. In order to get over this difficulty, the insoluble dye is treated with anhydrosulphuric acid, and thus converted into a mixture of sulphonic acids, the sodium salts of which are readily soluble, and come on the market under the names, '*Alkali blue*,' '*Water blue*,' &c.

In dyeing silk and wool with these colouring matters, the material is first dipped into alkaline solutions of the salts, when a light-blue tint is obtained, and it is not until it has been immersed in dilute acid (to liberate the sulphonic acid) that the true blue colour is developed. Cotton is dyed in the same way, but must first be mordanted with tannin.

The tri-hydroxy-derivatives of triphenyl carbinol and of tolyldiphenyl carbinol, which correspond with the tri-amino-compounds described above, may be obtained by treating the latter (the colour-bases of pararosaniline and of rosaniline) with nitrous acid, and then heating the solutions of the diazonium-salts. The products, *aurin* and *rosolic acid* respectively, correspond with the pararosaniline and rosaniline dyes in constitution:

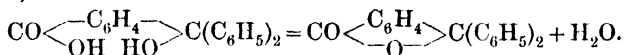


They are of little use as dyes, owing to the difficulty of fixing them.

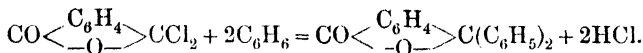
The Phthaleins.

The phthaleins, like malachite green and the rosanilines, are derivatives of triphenylmethane, inasmuch as they are substitution products of *phthalophenone*, a lactone (p. 263) formed from *tri-*

phenylcarbinol-o-carboxylic acid, by the loss of one molecule of water,

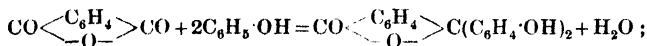


Phthalophenone is prepared by treating a mixture of phthalyl chloride (p. 458) and benzene with aluminium chloride,



It crystallises in colourless needles, melts at 115° , and dissolves in alkalis, yielding salts of triphenylcarbinol-o-carboxylic acid.

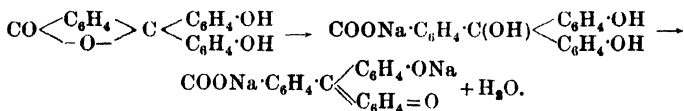
Phenolphthalein, $\text{C}_{20}\text{H}_{14}\text{O}_4$ (dihydroxyphthalophenone), is prepared by heating phthalic anhydride (3 parts) with phenol (4 parts) and anhydrous zinc chloride (5 parts), at $115\text{--}120^\circ$, during about eight hours,



the product is thoroughly extracted with boiling water (about 75 parts) and recrystallised from aqueous alcohol.

Phenolphthalein separates from alcohol in colourless crystals, and melts at about 250° ; it dissolves in dilute alkalis, giving solutions which have a deep-pink colour, owing to the formation of coloured salts, but on the addition of acids (or of concentrated alkali) the colour vanishes, hence the use of phenolphthalein as an indicator. It is, however, of no value as a dye.

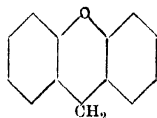
The conversion of colourless phenolphthalein into an intensely coloured salt may be ascribed to its transformation into a quinonoid compound, just as in the case of malachite green (p. 585),



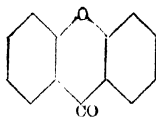
Xanthone Derivatives.

From the urine of oxen, which have been fed on mango-leaves, there is obtained in India a yellow pigment (*piuri*, *Indian yellow*) which is a magnesium salt of *euxanthic acid*, and which is decomposed by mineral acids, giving *euxanthone* and *glucuronic acid*,

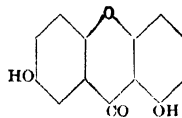
$\text{CHO}[\text{CH}\cdot\text{OH}]_4\cdot\text{COOH}$, a derivative of glucose. Euxanthone is a dihydroxyxanthone, and the parent substance of xanthone is the compound xanthene:



Xanthene.



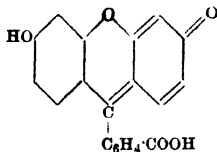
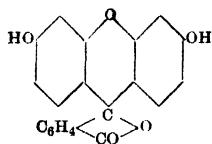
Xanthone.



Euxanthone.

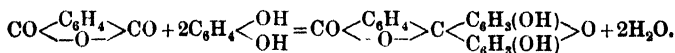
Xanthone (dipheno- γ -pyrone) is formed when *oo*-diaminobenzophenone is diazotised and the solution of the diazonium salt is heated, the *oo*-dihydroxybenzophenone, which is first formed, losing the elements of water; it is also produced when a mixture of phenol and salicylic acid is heated with concentrated sulphuric acid. It crystallises in colourless needles, melting at 173° .

Fluoresceins.—The fluoresceins are important dye-stuffs which are formed when phthalic anhydride is heated with *m*-dihydric phenols; they are derived from *fluoran*, a compound formed by the substitution of the complex, $\text{>C}<\begin{smallmatrix} \text{C}_6\text{H}_4 \\ \text{O}\cdot\text{CO} \end{smallmatrix}>$, for the >CH_2 group of xanthene, and are therefore closely related to the phthaleins, which are also derivatives of triphenylmethane, containing this lactone-complex. Their relationship to xanthene, xanthone, and fluoran is shown by the alternative structural formulæ for fluorescein given below,



of which the latter would accord better with the fact that fluorescein, unlike phenolphthalein, is itself coloured.

Fluorescein, $\text{C}_{20}\text{H}_{12}\text{O}_5$, the simplest member of this group, is produced by heating phthalic anhydride with resorcinol,



In this change, two hydrogen atoms of the two benzene nuclei

unite with the oxygen atom of one of the $>\text{CO}$ groups of the phthalic anhydride (as in the formation of phenolphthalein), and a molecule of water is also eliminated from the hydroxyl-groups of the two resorcinol molecules.

Phthalic anhydride (1 mol.) and resorcinol (2 mols.) are heated together at 200° until the mass becomes quite solid; the dark product is then thoroughly extracted with hot water, and recrystallised from aqueous alcohol.

Fluorescein separates from alcohol in dark-red crystals; it is almost insoluble in water, but dissolves readily in alkalis, forming dark, reddish-brown solutions, which, when diluted, show a very marked yellowish-green fluorescence (hence the name, fluorescein). In the form of its sodium salt, $\text{C}_{20}\text{H}_{10}\text{O}_5\text{Na}_2$, fluorescein comes into the market as the dye, '*uranin*.' Wool and silk are dyed yellow, and at the same time show a beautiful fluorescence, but the colours are faint, and soon fade; hence fluorescein has a very limited application alone, and is generally mixed with other dyes in order to produce fluorescent effects. Some of the derivatives of fluorescein are very important dyes.

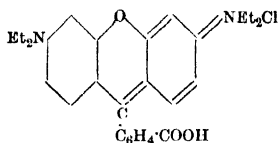
Eosin, $\text{C}_{20}\text{H}_8\text{O}_5\text{Br}_4$ (tetrabromofluorescein), is formed when fluorescein, suspended in alcohol, is treated with bromine, four atoms of hydrogen in the resorcinol nuclei being displaced. It separates from alcohol in red crystals, and is almost insoluble in water, but dissolves readily in alkalis, forming deep-red solutions, which, on dilution, exhibit a distinct green fluorescence, but not nearly to the same extent as solutions of fluorescein.

Eosin, in the form of its potassium salt, $\text{C}_{20}\text{H}_6\text{O}_5\text{Br}_4\text{K}_2$ (a brownish powder), is much used for dyeing silk, wool, cotton, and especially paper, which is coloured without the aid of a mordant. Silk and wool are dyed with eosin directly, in a bath acidified with acetic acid; but cotton must first be mordanted with tin, lead, or aluminium salts. The shades produced are a beautiful pink, and the materials also show a very noticeable fluorescence.

Tetraiodofluorescein, $\text{C}_{20}\text{H}_8\text{O}_5\text{I}_4$, is also a valuable dye. Its sodium salt, $\text{C}_{20}\text{H}_6\text{O}_5\text{I}_4\text{Na}_2$, is known as '*erythrosin*.'

Many other fluoresceins have been prepared by condensing substituted phthalic acids with other *m*-dihydric phenols, and then treating the products with bromine or iodine.

Rhodamines. --When phthalic anhydride is condensed with di-alkyl-derivatives of *m*-amino-phenols, tetra-alkyldiamino-substitution products of fluoran are produced. The salts of these compounds are beautiful red to bluish-violet basic dyes, which are strongly fluorescent; they may be represented by quinonoid structures, such as the following,



which correspond with those assigned to the fluoresceins.

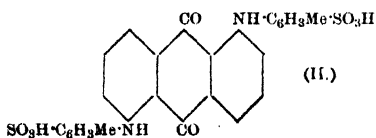
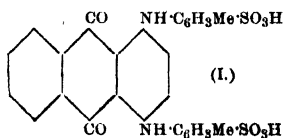
Derivatives of Anthracene.

Many derivatives of anthracene, in addition to alizarin (p. 498), are important dye-stuffs.

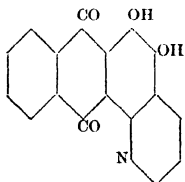
From alizarin itself, and from its isomerides, various tri-, tetra-, &c., hydroxyanthraquinones are prepared by oxidation with manganese dioxide and sulphuric acid.

Alizarin Bordeaux R, for example, is 1:2:5:8-tetrahydroxy-anthraquinone, and with aluminium mordants it gives claret-coloured dyes. **Alizarin cyanines**, mixtures of *penta*- and *hexa*-hydroxyanthraquinones, give violet-blue compounds in a similar manner.

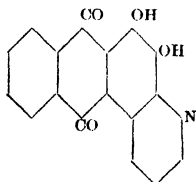
A different type of dye is obtained when a dihydroxy-, dinitro-, or dihalogen derivative of anthraquinone is heated with boric acid and an aromatic amine, and the product is then sulphonated in order to convert it into a soluble acid dye. When, for example, *quinizarin* (1:4-dihydroxyanthraquinone) is thus condensed with *p*-toluidine, both the hydroxy- are displaced by $\text{Me}\cdot\text{C}_6\text{H}_4\cdot\text{NH}-$ groups, and when sulphonated, the product gives **Alizarin cyanine green G** (I.); in a similar manner **Anthraquinone violet** (II.) is obtained from 1:5-substitution products of anthraquinone:



Another type of anthracene dyes is obtained when α - or β -nitroalizarin is heated with glycerol and concentrated sulphuric acid, whereby, just as in Skraup's reaction, a pyridine nucleus is generated; the compound (I.) thus formed from α -nitroalizarin is **Alizarin green**, and that (II.) from β -nitroalizarin is **Alizarin blue**:



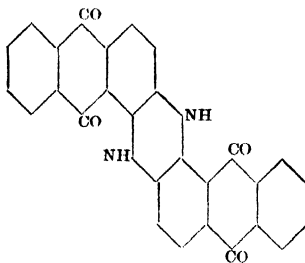
(I.)



(II.)

These dyes are used in conjunction with chromium mordants, but Alizarin blue can also be used as a vat dye (p. 583), and was, in fact, the first artificial vat dye to be prepared.

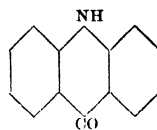
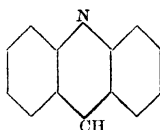
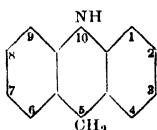
Indanthrene blue R is obtained by heating β -aminoanthraquinone with caustic potash at about 250° , two molecules of the amino-compound undergoing condensation, giving a molecule which contains 7 closed-chains. The product is a salt of the leuco-compound; it is dissolved in water, and air is passed through the solution in order to precipitate the indanthrene:



When indanthrene is reduced in alkaline solution it is converted into a soluble leuco-compound (compare anthraquinone, p. 497), which is readily oxidised by atmospheric oxygen, giving an insoluble blue dye; like indigo (p. 582) it can therefore be applied to fabrics as a vat dye. Several other indanthrene vat dyes, such as **Algol blue K**, the NN-dimethyl-substitution product of indanthrene blue, are manufactured; they are characterised by their fastness to light.

Acridine Derivatives.

Acridine, $C_{13}H_9N$, occurs in coal-tar anthracene (p. 328), to which it is closely related in constitution. It is a colourless, crystalline, feebly basic compound, which melts at 110° , and sublimes even at 100° ; solutions of acridine or of its salts show a blue fluorescence. It behaves like a tertiary base, and combines directly with methyl iodide, giving *methylacridonium iodide*; on oxidation with permanganate, it is converted into *acridinic acid* (quinoline-2:3-dicarboxylic acid), just as quinoline is converted into pyridine-2:3-dicarboxylic acid (p. 514), and on reduction it gives *dihydroacridine*:



Dihydroacridine can also be obtained by heating *oo*-diaminodiphenylmethane with acids; it is readily oxidised, giving acridine.

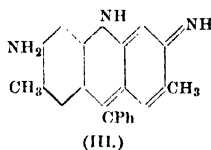
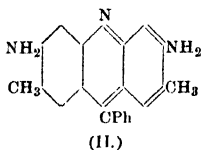
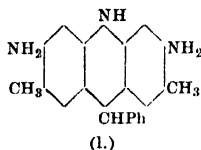
Acridine can be directly synthesised by heating diphenylamine with formic acid and zinc chloride, the N-formyl derivative of the base undergoing an inner condensation, with the loss of the elements of water: this is a general reaction, since by using other acids, many alkyl or aryl substituted acridines can be obtained.

2:8-Diaminoacridine sulphate (proflavine); a mixture of the hydrochlorides of *2:8-diaminoacridine* and *10-methyl-2:8-diaminoacridonium chloride* (acriflavine); and also a mixture of *2:8-diaminoacridine hydrochloride* and *10-methyl-2:8-diaminoacridonium chloride* (euflavine or acriflavine neutral), are all important antiseptics used in medicine and surgery.

Acridone, $C_{13}H_9ON$, can also be synthesised in various ways, as, for example, by heating *phenylanthranilic acid* (*phenyl-o-aminobenzoic acid*), $C_6H_5 \cdot NH \cdot C_6H_4 \cdot COOH$, with sulphuric acid at 100° ; it melts at 354° , and towards methyl iodide behaves like a secondary base, giving *N-methylacridone*. When strongly heated with zinc-dust, it is reduced to acridine.

Dyes, derived from acridine, may be obtained by condensing aldehydes with *m*-diamines, and oxidising the products with ferric chloride; they usually show a marked green fluorescence.

Benzoflavin, for example, is formed when *m*-toluylenediamine, $C_6H_3Me(NH_2)_2[2NH_2=2:4]$, is condensed with benzaldehyde, and the product (I.), formed with the loss of the elements of ammonia, is oxidised; the structure of the oxidation product may be represented by one of the quinonoid formulæ, II. or III., and the dye is a salt of the base:

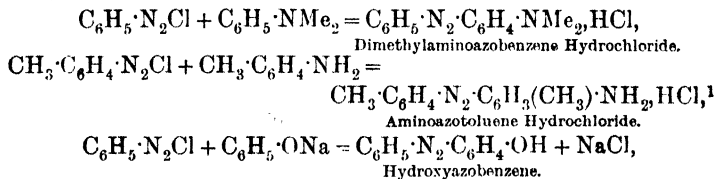


Acridine yellow R is obtained in a similar manner, using formaldehyde in the place of benzaldehyde, whereas **Acridine orange R** is prepared from *dimethyl-m*-phenylenediamine and benzaldehyde.

Azo-Dyes.

The azo-dyes contain the chromophore, $-N:N-$, to each of the nitrogen atoms of which a benzene, naphthalene, or other benzenoid nucleus is directly united. Azobenzene, $C_6H_5 \cdot N_2 \cdot C_6H_5$, the simplest aromatic azo-compound, although coloured, is not a dye (compare p. 579); when, however, one or more hydrogen atoms of azobenzene are displaced by amino-, hydroxyl-, or sulphonic-groups (auxochromes, p. 584), the products, as, for example, aminoazobenzene, $C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot NH_2$, hydroxyazobenzene, $C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot OH$, azobenzenesulphonic acid, $C_6H_5 \cdot N_2 \cdot C_6H_4 \cdot SO_3H$, are soluble in acids or in alkalis, and are yellow or brown dyes.

Azo-dyes are usually prepared by the process of 'coupling' (p. 410), namely, by treating a diazonium-salt with an amino-compound or with a phenol,



¹ In cases where a diazoamino-compound is first produced, an excess of the amino-compound is employed, and the mixture is gently warmed until the change into the aminoazo-compound is complete (compare p. 408).

These equations show the formation of very simple azo-compounds only. Substituted diazonium-salts, not only of benzene, but of naphthalene and other aromatic hydrocarbons, may be coupled with substituted amino- and phenolic-derivatives of such hydrocarbons, with the production of many different basic or acidic (*mono*)-azo-dyes. Further, when this dye is an amino-compound, it may be diazotised, and its diazonium-salt may then be coupled with another amino- or phenolic-derivative of benzene or naphthalene; the molecule of the compound thus formed contains two $-N_2-$ groups, and is a *dis-azo*-dye, of the type, $X \cdot N_2 \cdot X \cdot N_2 \cdot X$, where X represents any substituted benzenoid nucleus. By a repetition of such operations, and in other ways (p. 599) *tris-azo*- and *tetrakis-azo*-dyes, containing three and four $-N_2-$ groups respectively, may be obtained, and theoretically such processes can be continued indefinitely. Since there are so many derivatives of benzene and of naphthalene, which can be coupled, it is not surprising that many thousands of azo-dyes have been prepared; theoretically, from the known intermediates, millions might be obtained.

In all these reactions, the $-N_2-$ group displaces hydrogen of the benzene nucleus from the *p*-position to one of the amino- or hydroxyl-groups; when the *p*-position is occupied, the $-N_2-$ group displaces hydrogen from the *o*-position, but not so readily; when both *p*- and *o*-positions are occupied, no reaction occurs as a rule, but in some cases a carboxyl-radical in the *p* position is actually displaced by the $-N_2-$ group. 1-Hydroxy- and 1-amino-derivatives (*α*-derivatives) of naphthalene couple in the 4-position, but when the 4- or the 3-position is occupied, the $-N_2-$ group displaces hydrogen from the 2-position. When the 2- and 4-positions are both occupied, there is no reaction. 2-Hydroxy- and 2-amino-compounds (*β*-derivatives) couple in the 1-position, and when this is occupied no reaction takes place as a rule.

The technical operations involved in the production of azo-colours, as a rule, are very simple. In coupling diazonium-compounds with phenols and their derivatives, the amino-compound (1 mol.) is diazotised, and the solution of the diazonium-salt is then slowly run into the cold *alkaline* solution of the phenol, or its sulphonic acid, care being taken to keep the solution slightly alkaline, otherwise interaction ceases, owing to the presence of liberated acid. In the case of amino-compounds, the aqueous solution of the diazonium-salt is added to that

of the salt of the amino-compound (compare footnote, p. 597), in the presence of sodium acetate or formate; in some cases, however, the reaction takes place in alcoholic solution only.

The dye, having been precipitated with acid, alkali, or salt, if necessary, is separated in filter-presses, dried, ground, and standardised.

The process of coupling may be carried out within the fibres of a material, so that no mordant is required, even for cotton. When, for example, a piece of calico, which has been soaked in an alkaline solution of β -naphthol and then wrung out, is dipped into a solution of diazotised *p*-nitroaniline, the insoluble dye, *p*-nitroaniline red (*Para-red*) is formed within the fibres (*Ice-colour* process). In another method the material is impregnated with an amino-compound, which is diazotised, and then coupled with the necessary substance to produce the desired dye (*Ingrain dyes*).

When the amino-compound is only very sparingly soluble in water, it may be converted into a readily soluble derivative, from which it is easily regenerated within the fibres.

Aminoazobenzene, for example, can be converted into a readily soluble sulphonic acid, $\text{C}_6\text{H}_5\cdot\text{N}_2\cdot\text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{CH}_2\cdot\text{SO}_3\text{H}$; when fibres, impregnated with this compound are warmed with dilute acids or alkalis, the regenerated base is retained by the fibres and can be subsequently diazotised and coupled.

Unstable side-chain sulphonic acids thus used, principally in dyeing cellulose acetate, are called *ionamines*.

Such *development processes* are also used on materials which have already been *dye*d with some basic dye-stuff; or the material is dyed with some azo-compound, which is afterwards treated with a solution of some diazonium-salt. By these methods, di-, tri-, &c. azo-dyes of high quality are formed; some of the diazonium compounds required for such purposes are supplied to dyers in the form of soluble powders, which consist of 'stabilised' derivatives (p. 602).

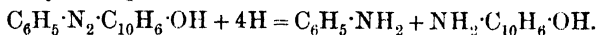
Acid azo-colours (hydroxy- and sulphonic-derivatives) are taken up by animal fibres directly from an acid bath, and are principally employed in dyeing wool; they can be fixed on cotton with the aid of mordants (tin and aluminium salts being generally employed), but, as a rule, only with difficulty; some azo-dyes, notably those of the *congo-group* (p. 603), dye cotton directly without a mordant.

Basic azo-dyes are readily fixed on cotton which has been

mordanted with tannin, and are used in dyeing calico and other cotton goods.

From the equations given above (p. 597) it might be concluded that the process of coupling is a simple double decomposition. It is probable, however, that an additive compound is first formed, and that the displacement of hydrogen of the nucleus by the $-N_2-$ group is a secondary reaction; further, the azo-compound thus formed may then undergo an isomeric change. The product of the interaction of phenyldiazonium chloride and β -naphthol, for example, is insoluble in alkalis, and apparently, therefore, is not a phenol of the constitution, $C_6H_5 \cdot N_2 \cdot C_{10}H_6 \cdot OH$; it is identical with the compound produced by the action of phenylhydrazine on β -naphthaquinone, which presumably has the structure, $C_6H_5 \cdot NH \cdot N : C_{10}H_6 : O$. It must be concluded, therefore, that benzeneazonaphthol passes into this hydrazone by an isomeric change. Similar transformations probably occur in the case of many (but not all) other azo-compounds, especially in those in which the $-N_2-$ group is in an *o*-position to a hydroxyl- or amino-group.

When azo-dyes are treated with reducing agents they are first converted into colourless, or only slightly coloured, hydrazo-compounds, the chromophore, $-N_2-$, being transformed into $-NH-NH-$. More energetic treatment brings about further reduction and the $-NH-NH-$ group is transformed into $-NH_2 \cdot NH_2-$, so that the two benzenoid nuclei of the azo-compound are no longer united and two (identical or) different amino-compounds are formed; in the case of benzeneazonaphthol, the final change may be expressed by the equation



By identifying the products of reduction, the structure of the azo-dye would be determined. In the case of those containing two, three, or more $-N_2-$ groups, mixtures of three, four, or more amino-compounds would be obtained, and the identification of these reduction products might either establish the constitution of the dye, or at least show from what components it had been formed, but not necessarily the order in which they had been coupled.

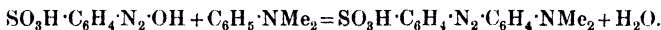
Chrysoidine, $C_6H_5 \cdot N_2 \cdot C_6H_3(NH_2)_2$ (diaminoazobenzene), is produced by mixing molecular proportions of phenyldiazonium

chloride and *m*-phenylenediamine (p. 395) in aqueous solution. The hydrochloride crystallises in reddish needles, is moderately soluble in water, and dyes silk and wool directly, and cotton mordanted with tannin, an orange-yellow colour.

Bismarck brown is prepared by treating *m*-phenylenediamine hydrochloride with nitrous acid; a part of the base is converted into a mono-diazonium-compound, which then couples with some unchanged base giving triaminoazobenzene, $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_3(\text{NH}_2)_2$, but at the same time, there is formed a tetra-azonium-salt, which reacts in a similar manner with two molecules of the diamine, giving a *dis*-azo-compound, $(\text{NH}_2)_2\text{C}_6\text{H}_3 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_3(\text{NH}_2)_2$. The dye is a mixture of these two substances.

The hydrochloride is a dark-brown powder, and is largely used in dyeing cotton (mordanted) and leather a dark brown.

Helianthin (dimethylaminoazobenzenesulphonic acid) is prepared by mixing aqueous solutions of diazotised sulphanilic acid and dimethylaniline hydrochloride,



Sulphanilic acid (2 mols.) is dissolved in a solution of sodium carbonate (1 mol.), sodium nitrite (2 mols.) is added, and the mixture is cooled to about 5°. Hydrochloric acid (2 mols.) is run in slowly (from a burette), and then a solution of dimethylaniline (2 mols.) in the theoretical quantity of dilute (1:3)hydrochloric acid. The sulphonic derivative of the azo-compound is then treated with a slight excess of caustic alkali, and after a short time the sodium salt is separated by filtration and recrystallised from boiling water. Starting with 5 g. of sulphanilic acid, the volume of the final alkaline solution should be 80–100 c.c.

The sodium salt (*methylorange*) forms orange-yellow crystals, and its yellow aqueous solution is coloured red on the addition of acids, owing to the formation of a salt with the acid; hence its use as an indicator. It is seldom employed as a dye, on account of its sensibility to traces of acid.

Resorcin yellow (Tropæolin O) is prepared by diazotising sulphanilic acid and coupling it with resorcinol, and has the constitution, $\text{SO}_3\text{H} \cdot \text{C}_6\text{H}_4 \cdot \text{N}_2 \cdot \text{C}_6\text{H}_3(\text{OH})_2$. Its sodium salt is a moderately brilliant orange-yellow dye, and is not readily acted on by acids; it is chiefly employed, mixed with other dyes of similar constitution, in the production of olive-greens, maroons, &c.

By using various other benzene derivatives, and coupling them, as in the above examples, *yellow* and *brown* dyes of almost

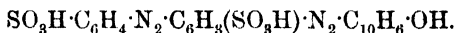
any desired shade can be obtained; in order, however, to produce a *red* azo-dye, a compound containing at least one naphthalene nucleus must be prepared. The dyes thus obtained give various shades of reddish-brown or scarlet, and are known collectively as 'Ponceaux' or 'Bordeaux.'

When, for example, xylyldiazonium chloride is combined with β -naphtholdisulphonic acid, a scarlet dye (**Scarlet R**) of the composition, $C_6H_3Me_2 \cdot N_2 \cdot C_{10}H_4(SO_3H)_2 \cdot OH$, is formed; another scarlet dye (**Ponceau 3R**) is produced by the interaction of pseudocumyldiazonium chloride and β -naphtholdisulphonic acid, and has the composition, $C_6H_2Me_3 \cdot N_2 \cdot C_{10}H_4(SO_3H)_2 \cdot OH$.

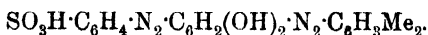
Paranitroaniline red, $NO_2 \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_6 \cdot OH$, is an important azo-dye, which is applied to cotton fabrics in the manner already described (p. 599); the 'stabilised' diazonium-derivative required in this operation is sold under the name of '*nitrosamine red*,' and is not an ordinary diazonium-salt, but a sodium derivative, $NO_2 \cdot C_6H_4 \cdot N_2 \cdot ONa$ or $NO_2 \cdot C_6H_4 \cdot NNa \cdot NO$, which, when treated with acids, is converted into *p*-nitrophenyldiazonium-salts.

Rocellin, $SO_3H \cdot C_{10}H_6 \cdot N_2 \cdot C_{10}H_6 \cdot OH$, a compound produced by coupling β -naphthol with the diazonium-compound of naphthionic acid (p. 486), may be mentioned as an example of an azo-dye containing two naphthalene nuclei. It gives beautiful red shades, very similar to those obtained with the natural dye, cochineal, which rocellin and various allied azo-colours have, in fact, almost superseded.

Dis-azo-dyes may be prepared in various ways. (1) An amino-azo-compound may be diazotised and coupled with one molecule of an amino- or phenolic-derivative; aminoazobenzenedisulphonic acid, for example, diazotised and coupled with β -naphthol, gives **Biebrich scarlet**,



(2) A phenolic or amino-compound may be coupled with two molecules of the same or of different diazonium salts; resorcinol, treated in this way with diazosulphanilic acid and with xylyldiazonium chloride, gives **Resorcin brown**,



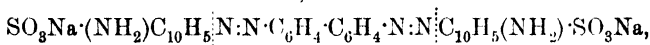
(3) A diamino-compound such as *m*-phenylenediamine (p. 395) or 1:5-diaminonaphthalene may be tetrazotised (converted into

a bis-diazonium or tetra-azonium-salt) and coupled with two molecules of the same or of different benzenoid nuclei.

Many important dyes are prepared by this last method from benzidine (p. 411) and substitution products of this base, such as *tolidine*, *dianisidine*, *diphenetidine*,¹ and since the tetrazo-derivatives react readily with one molecule, and only slowly with a second molecule, of the amino- or phenolic-compound, it is relatively easy to prepare many dis-azo dyes, $A \cdot N_2 \cdot C_6H_4 \cdot C_6H_4 \cdot N_2 \cdot B$, in which A and B represent the same or different substituted aromatic nuclei; similarly in the case of substitution products of tetrazotised benzidine.

The first dye thus obtained from benzidine was *Congo red*, and the compounds of this group, of which some hundreds are known, are classed as dyes of the Congo-group; they are direct dyes to (unmordanted) cotton, and were the first dyes, having this important property, to be discovered. They are much used in the dyeing of wood, paper, leather, &c., as well as for fabrics.

Congo red, produced by coupling diphenyltetra-azonium chloride with naphthionic acid (p. 486) is one of the important compounds of this class. Its sodium salt,



is a scarlet powder, which on the addition of acids turns blue, owing to the formation of a salt with the acid.

Tolidine, and to a greater extent *dianisidine*, give rise to bluer shades of red than does benzidine, with naphthionic acid, and when the tetrazotised bases are coupled with phenolic instead of with amino-sulphonic acids, blue, instead of red dye-stuffs are obtained, as will be seen from the following table:

Name of Dye.	Tetrazotised Base.	Compound, or Compounds, coupled with the Tetrazotised Base.
Congo red (scarlet)	Benzidine	{ Naphthionic acid. Naphthionic acid.
Benzopurpurin 4B (blue red)	Tolidine	{ Naphthionic acid. Naphthionic acid.

¹ *Tolidine*, $NH_2 \cdot MeC_6H_3 \cdot C_6H_3Me \cdot NH_2$, *dianisidine* (*dimethoxybenzidine*), and *diphenetidine*, $NH_2 \cdot (OEt)C_6H_4 \cdot C_6H_4(OEt) \cdot NH_2$, are produced from o-nitro-toluene, o-nitroanisole, and o-nitrophenetole respectively, by reactions similar to those by which benzidine is produced from nitrobenzene; when their salts are treated with nitrous acid, they yield tetra-azonium-compounds, just as benzidine gives salts of diphenyltetra-azonium hydroxide.

Name of Dye.	Tetrazotised Base.	Compound, or Compounds, coupled with the Tetrazotised Base.
Benzopurpurin 10B (blue red)	Dianisidine	{ Naphthionic acid. Naphthionic acid.
Congo corinth B (violet)	Tolidine	{ Naphthionic acid. α-Naphtholsulphonic acid.
Azo blue (blue violet)	Tolidine	{ α-Naphtholsulphonic acid. α-Naphtholsulphonic acid.
Benzoazurine G (pure blue)	Dianisidine	{ α-Naphtholsulphonic acid. α-Naphtholsulphonic acid.

Various Colouring Matters.

Naphthol yellow, $C_{10}H_5(NO_2)_2 \cdot OH$ (2:4-dinitro-naphthol), is obtained by the action of nitric acid on α-naphtholmono- or disulphonic acid, the sulphonic group or groups being displaced during nitration. The dye is the sodium salt, $C_{10}H_5(NO_2)_2 \cdot ONa$; it is readily soluble in water, and dyes silk and wool directly an intense golden yellow.

When α-naphtholtrisulphonic acid is nitrated, only two of the sulphonic groups are eliminated, and the resulting substance, $C_{10}H_4(NO_2)_2(OH) \cdot SO_3H$, is the sulphonic acid of naphthol yellow. This dye is called **Naphthol yellow S**, and is used in the form of its potassium salt, $C_{10}H_4(NO_2)_2(OK) \cdot SO_3K$, which gives yellow shades, faster to light than those of naphthol yellow.

The fact that these and some other nitrophenols, such as o-nitrophenol and picric acid, are coloured, whereas trinitrobenzene and trinitrotoluene, for example, are colourless, can be explained by assuming that the coloured compounds are quinonoid in structure, as the result of isomeric change; there is independent evidence in favour of such a view.

Mauveine, $C_{27}H_{24}N_4 \cdot HCl$ (*mauve*), is of historical interest (p. 578) and was first obtained by oxidising a salt of commercial aniline (containing toluidine) with potassium dichromate; from pure aniline, Perkin obtained *pseudomauveine*, $C_{24}H_{18}N_4 \cdot HCl$, which is now known to be a *quinone-imine* dye-stuff of the constitution,



and of which mauveine is a trimethyl-derivative. These com-

pounds were at one time used for colouring penny stamps, but are no longer of any practical importance.

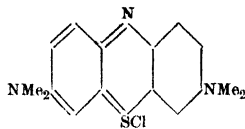
Aniline black is a highly complex insoluble compound, which is produced when an aniline salt is oxidised with potassium dichromate and an acid; the presence of traces of copper or vanadium salts, or of ferrocyanide, hastens the oxidation, which may even be brought about with atmospheric oxygen in the presence of a trace of *p*-phenylenediamine, as well as that of a copper salt. On oxidation with potassium dichromate and sulphuric acid, aniline black gives quinone (p. 445), and its molecule probably consists of aniline residues, which have combined with the loss of hydrogen, forming chains of quinonoid complexes. Aniline black is an important fast black dye, especially for cotton, and being insoluble, it must be produced within the fibres of the material.

Methylene blue, $C_{16}H_{18}N_3ClS$, was first prepared by the oxidation of dimethyl-*p*-phenylenediamine (p. 397) with ferric chloride, in the presence of hydrogen sulphide.

Nitrosodimethylaniline (p. 397) is reduced in strongly acid solution with zinc-dust, or with hydrogen sulphide, and the solution of dimethyl-*p*-phenylenediamine, thus obtained, is treated with ferric chloride in the presence of excess of hydrogen sulphide. The intensely blue solution, thus produced, is mixed with salt and zinc chloride, which precipitate the colouring matter as a zinc double salt.

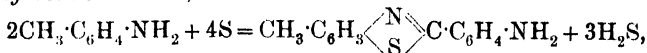
Methylene blue is readily soluble in water, and is a valuable cotton-blue, as it dyes cotton, mordanted with tannin and tartar emetic, a beautiful blue, which is very fast to light and soap; it is not much used in dyeing silk or wool, but it is extensively employed in staining biological preparations.

The structure of methylene blue (as the chloride) is expressed by the following quinone-imine formula, which corresponds with that assigned to pseudomauveine:

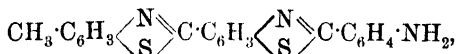


Primuline is a mixture of two or more compounds manufactured by heating *p*-toluidine with sulphur and then sulphonating the

product. The first changes which occur lead to the formation of *dehydrotoluidine*,



which then reacts with another molecule of *p*-toluidine and 4 atoms of sulphur, as before, to form *bis-dehydrotoluidine*,



and more complex compounds; the mixture is then sulphonated, the $-\text{SO}_3\text{H}$ group displacing hydrogen from the $\text{NH}_2\cdot\text{C}_6\text{H}_4-$ complex. The sodium salts of the sulphonic acids dye cotton directly a greenish-yellow colour, and are of little importance; but when the dyed fabric is afterwards treated with nitrous acid, and the resulting diazonium-salts are coupled with various phenolic compounds, yellow, orange, red, &c., ingrain azo-dyes (p. 599) are obtained.

Diazotised primuline is decomposed by light; when an impregnated material is exposed under a negative and then 'developed' with a phenol, the depth of colour due to the formation of an azo-compound will vary according to the extent to which decomposition has occurred.

Indigo, $\text{C}_{16}\text{H}_{10}\text{O}_2\text{N}_2$, is a natural dye which has been used from the earliest times. It was obtained from the leaves of the indigo-plant (*Indigofera tinctoria*) and from woad (*Isatis tinctoria*), which contain *indican*, $\text{C}_8\text{H}_6\text{ON}\cdot\text{C}_6\text{H}_{11}\text{O}_6$, a colourless, crystalline glucoside of indoxyl (p. 525). When the leaves are macerated with water fermentation sets in, and the glucoside is hydrolysed into glucose and indoxyl; on exposure to the air the indoxyl in solution undergoes atmospheric oxidation, and indigo separates as a blue scum.

Indigo (*indigotin*) is now prepared synthetically, starting from naphthalene (below); it is a dark-blue crystalline substance which, especially when rubbed, shows a copper-like lustre. It is insoluble in water and most other solvents, but dissolves readily in hot aniline, from which it may be crystallised.

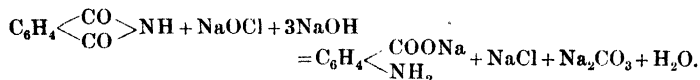
Alkaline reducing agents convert indigotin into its leuco-compound, *indigo-white*, which, in contact with the air, is rapidly reconverted into indigo-blue (indigotin), a property made use of in dyeing with this substance (p. 582); fuming sulphuric acid dissolves indigotin, with the formation of *indigodisulphonic acid*,

$C_{16}H_8O_2N_2(SO_3H)_2$, the sodium salt of which is used in dyeing under the name 'indigo carmine.'

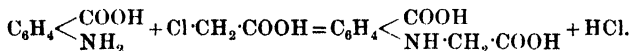
The great value of indigo (indigotin) in the dye industry naturally made it an attractive subject for investigation, and as the result of laborious research on the part of many chemists, the constitution of indigotin was established about 1880, chiefly by the work of Baeyer and his pupils. During his investigations, Baeyer succeeded in preparing indigotin artificially by various reactions, two of which have already been described (pp. 441, 466), but it was not until about 1900 that successful processes for the manufacture of indigotin had been worked out in Germany; since that time synthetic indigotin has gradually displaced the natural product of the indigo-plantations.

The most important of these methods was based on a discovery of Heumann, who found that indigotin could be obtained by heating phenylglycine (phenylaminoacetic acid) with alkalis in the presence of air, and the whole process may be summarised as follows: Naphthalene is oxidised to phthalic anhydride by heating it with sulphuric acid in the presence of mercuric sulphate, or by atmospheric oxidation at 440–480° in the presence of a catalyst (p. 457). Phthalic anhydride is converted into phthalimide (p. 458) by heating it with ammonia under pressure.

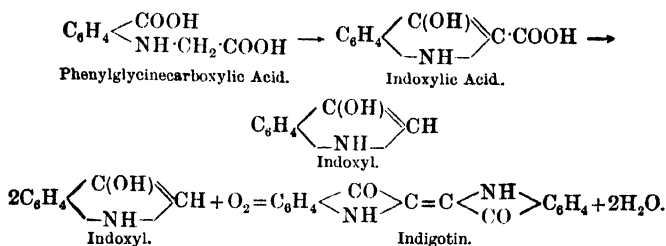
Phthalimide is converted into anthranilic acid (o-aminobenzoic acid, p. 455) by treating it with an alkali hypochlorite, a method discovered by Hoogewerf, which is analogous to that used by Hofmann in transforming amides into amines (p. 193),



Anthranilic acid is treated with chloroacetic acid to obtain phenylglycine-o-carboxylic acid,

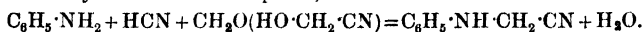


This compound, like phenylglycine itself, is converted into indigotin when it is fused with a mixture of caustic potash and caustic soda, the change taking place in several stages: The last reaction is carried out by dissolving the fused mass in water and passing a stream of air through the alkaline solution.



Many derivatives of indigotin, such as its halogen substitution products, and *thioindigotin* (a compound in which each of the $>\text{NH}$ groups of indigotin has been displaced by an atom of sulphur) are now manufactured and used as vat dyes.

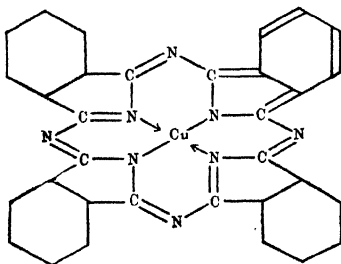
Anthranilic acid is now used instead of phenylglycinecarboxylic acid, and is obtained by the hydrolysis of its *nitrile*, which is manufactured by treating aniline with a mixture of sodium cyanide and formaldehyde sodium bisulphite,



The acid is then fused with a mixture of sodamide and caustic alkali.

Phthalocyanines.

The metallic phthalocyanines are very important organic pigments. Their discovery was due to the formation of patches of a blue substance in some phthalimide, which had been prepared by passing ammonia into phthalic anhydride, contained in an iron pan. Linstead and his co-workers then showed that this blue compound was *iron phthalocyanine*, and prepared analogous pigments by heating *o*-cyanobenzamide with a metal or an appropriate salt; of these, *copper phthalocyanine*, the structure of which is shown below, is now manufactured by heating phthalonitrile,



$C_6H_4(CN)_2$, with copper at 220–270°, and is known as **Monastral Fast Blue**, B.S.

This compound sublimes at 550° under reduced pressure, is insoluble in, and unchanged by, acids and alkalis, and is very fast to heat and to light; it can be sulphonated and thus converted into a soluble product, used as a *dye* for paper.

Monastral Fast Green, G.S., is a derivative of copper phthalocyanine in which all the sixteen hydrogen atoms are displaced by atoms of chlorine. **Lead phthalocyanine** is also green.

The metallic phthalocyanines are not dyes, but pigments; they are used as paints or enamels for colouring wall-paper, leather, cloth, linoleum, rubber, plastics, etc.

Note on the Identification of Organic Compounds.

Practice in the identification of organic compounds in the laboratory is of great help to the student in his theoretical work, and also trains his powers of observation; conclusions based on inaccurate observations are, of course, fatal to success.

Only a very small proportion of carbon compounds can be identified by qualitative tests; a larger number can be referred to their type or class, but for the vast majority—which are therefore unsuitable for such purposes—the quantitative methods, described in Chapter I., would have to be adopted.

The substances usually chosen for such exercises—to which alone this note applies—may be broadly classed in two groups:

I. Those which can be identified directly, as, for example, some of the simpler halogen derivatives, alcohols, aldehydes, ketones, and acids of the aliphatic series; aromatic hydrocarbons, nitro- and amino-compounds, phenols, and acids; and a few of the sugars (and glucosides) and alkaloids.

II. Those which must first be hydrolysed to give recognisable compounds of Group I., as, for example, esters, amides, and anilides. Salts, mineral or otherwise, may be classed in either group (p. 612).

The methods of examination have little in common with those of inorganic qualitative analysis; no tables are (or should be) used, and no fixed procedure is necessarily adopted. A few simple tests, occupying a few minutes only, serve as a guide

to further investigation, but the interpretation of the results, throughout the whole of the work, requires some considerable theoretical knowledge.

The colour and smell of the compound are noted. Only a **very few** substances (nitro-compounds, quinones) are coloured, but many commercial products, especially bases, are yellow or brown owing to the presence of impurities. Many types of compounds (hydrocarbons, halogen compounds, ketones, aldehydes, phenols, acids, and esters) have a distinctive class, or individual, odour, the recognition of which is greatly improved by a little practice.

The following tests may then be made :

1. The substance is heated in the Bunsen flame. If it burns with a feebly luminous flame, it is probably rich in oxygen (e.g. methyl alcohol, oxalic acid, glycerol); a smoky flame indicates a high proportion of carbon (aromatic compounds generally) or the presence of halogen.

2. The compound, liquid or solid, is heated in a test-tube. If it distils, a very rough observation of its boiling-point may often be made by holding a thermometer bulb in the vapour; a boiling-point below 81° shows the absence of all aromatic compounds (benzene boils at 81°). If it decomposes, all the above-named types of Group I. which contain only *one* characteristic group are excluded; decomposition, without appreciable charring, indicates simple aliphatic compounds, containing two characteristic groups, such as hydroxy- and dicarboxylic-acids, but if charring occurs the presence of more complex hydroxy-acids (sulphonic acids), sugars (glucosides), or alkaloids is indicated, and, in general, compounds of very high molecular weight. Metallic salts of simple acids (formic, acetic, oxalic, benzoic) do not char appreciably, but salts of the alkaloids and of many organic bases carbonise readily. When in this test, or in (1), the substance does not volatilise *completely*, it should be ignited on a porcelain crucible-lid; a *non-combustible* residue shows a metallic salt (p. 14), and the further procedure is described on (p. 612).

3. The substance is treated with cold water (note comparative density). If it is readily or moderately soluble (footnote, p. 148), the presence of one or more $-\text{OH}$, $-\text{COOH}$, $-\text{CO}\cdot\text{NH}_2$, $-\text{SO}_3\text{H}$, $-\text{NH}_2$, $-\text{CHO}$, or $>\text{CO}$ groups is indicated, but the solubility

must be considered in conjunction with the results of (2). If, for example, the compound decomposes when it is heated, it cannot owe its solubility to *one* of these groups only (except $-\text{SO}_3\text{H}$); on the other hand it might be sparingly soluble and yet contain one of these groups in combination with a hydrocarbon radical (such as $\text{C}_5\text{H}_{11}-$ or C_6H_5-) of fairly high molecular weight. Hydrocarbons (ethers), halogen compounds, nitro-derivatives, and most esters (p. 172) are very sparingly soluble in water.

4. The substance is treated with a cold solution of (a) sodium carbonate, (b) caustic soda, (c) hydrogen chloride. If it is more readily soluble in (a) than in water, it is probably an acid, anhydride, or nitrophenol (yellow); effervescence *may* not be detected if the substance dissolves very slowly, as the carbon dioxide may form bicarbonate, but may generally be observed when the compound is added to a *hot* solution of sodium carbonate. If it is more readily soluble in (b) than in (a), it is probably a phenol. If more soluble in (c) than in (a) or (b), it is very probably a base (or a *salt*, below).

The results of these few simple tests *considered as a whole*, in the case of substances of Group I., will often give some definite indication, which can then be followed up.

Example.—An odourless solid decomposes when it is heated, leaving no residue, but does not char. Its decomposition products are not recognised by their smell. The substance is readily soluble in cold water, and dissolves in sodium carbonate solution with effervescence. It cannot be a simple monocarboxylic acid, but it might be a simple hydroxy- or dicarboxylic acid, and further tests are made for the individual compounds of these types.

Example.—A liquid has a 'basic' smell, distils at $175-185^\circ$,¹ is only moderately soluble in water and aqueous alkali, but dissolves readily in diluted (1:1) hydrochloric acid, and is reprecipitated from the (sufficiently concentrated) solution on the addition of an alkali. It is therefore a base (not an alkaloid), and tests are immediately made to find out whether it is a primary, secondary, or tertiary base and whether it is an aromatic or an aliphatic compound (pp. 200, 396, 403).

Example.—A liquid, smelling like 'carbolic acid,' distils at $178-188^\circ$;¹ it is only moderately soluble in cold water, and in sodium carbonate solution, but dissolves in caustic soda and is reprecipitated from the (sufficiently concentrated) solution on the addition of an acid. It is probably a phenol, and is tested further with ferric chloride and by Liebermann's reaction (pp. 423, 424).

¹An approximate result, observed in a test-tube experiment.

Example.—An odourless solid, distils at a high temperature (above 200° apparently); it is readily soluble in cold water, and when treated with a solution of sodium carbonate the liquid begins to turn yellow, and darkens rapidly when shaken (in contact with the air). Probably a di- or poly-hydric phenol (pp. 431–433).

When the above tests (1–4), which may be carried out in any order, have failed to give any clue to its nature, the compound probably belongs to Group II. (amides, anilides, esters), and its examination may proceed as follows:

5. The substance is heated with a concentrated solution of caustic soda. If it is an ammonium salt or an amide (or a cyanide) ammonia will be evolved. The substance is then mixed with solid sodium carbonate and the mixture is moistened with water; an immediate evolution of ammonia shows an ammonium salt, the presence of which may have already been suspected from the results of (2), (3), or (4). Amides (and cyanides) may be hydrolysed only very slowly (reflux apparatus); the acid which is formed is identified as described under esters (p. 173). If the substance is a substituted amide (anilide) it will gradually undergo hydrolysis, giving a primary base and the salt of an acid; the base, which usually separates as an oil, may be extracted with ether; the acid is identified as before. Certain anilides are very stable towards boiling alkalis, and are more easily hydrolysed with boiling diluted (1:1) sulphuric acid; the free organic acid and a salt of the base are thus obtained.

The hydrolysis of esters, for their identification, has already been described (p. 172).

(6) When at this stage no satisfactory clue has been obtained the substance may be tested for nitrogen, halogens, and sulphur (pp. 14–16). If nitrogen is found, and the compound is not one of the types already considered, it may be a nitro-derivative or some compound such as sulphanilic acid (p. 419) or hippuric acid (p. 451). A nitro-derivative can be reduced and the base identified. If a halogen is found, its nature is determined and, if necessary, the substance is heated with an aqueous-alcoholic solution of silver nitrate (pp. 69, 374). If sulphur is found, the compound may be an alkyl hydrogen sulphate (as a salt), a sulphonic acid, or a sulphonamide (which might not have been detected under 5); the sulphonic derivatives are fused with alkalis and converted into phenols (p. 422).

7. *Salts*.—If the substance is a salt of any kind some indications of this should have been obtained in one or more of the preceding tests. A metallic or ammonium salt may be treated with diluted sulphuric acid and the solution examined, as described under esters (p. 173). Salts of organic bases (*which may be mistaken for organic acids*) are treated with an excess of alkali, and the liberated base is extracted with ether, if necessary; the alkaline solution is examined for inorganic and organic acids.

8. If all the above tests have failed to give any definite information, the substance may be treated with phenylhydrazine (p. 407), or strongly heated with soda-lime, concentrated sulphuric acid, or oxidising agents.

Example.—A pleasant-smelling liquid (b.p. 55–65°),¹ is not appreciably soluble in water, alkalis, or acids, and does not *seem* to be changed when it is heated with these reagents. It is observed that its density is very much greater than that of water; possibly a halogen compound. It is tested for halogens and proved to contain chlorine; probably chloroform (p. 72).

Example.—An odourless solid distils (b.p. above 200°). It is sparingly soluble in cold water, alkalis, and acids. When heated with caustic soda it seems to give a basic odour (not ammonia). Probably an anilide. It is boiled with diluted (1:1) sulphuric acid (reflux condenser), and after a short time the vapours in the flask are found to have an acid reaction and a smell of acetic acid. The heating is continued during, say, 30–60 minutes, and the volatile, readily soluble acid is identified; the sulphuric acid solution is examined for a primary aromatic base.

Example.—A liquid (distinct odour, but not recognised), burns with a smoky flame, boils at about 105–115°, and is practically insoluble in, and apparently unchanged by, water, alkalis, or acids. Nitrogen, halogens, and sulphur are absent, but, in carrying out the test, it is seen that the boiling liquid and the sodium do not interact. Probably an aromatic hydrocarbon (toluene?). Treated with a mixture of nitric and sulphuric acids, the substance, itself lighter than water, gives an oil denser than water. This product is treated with tin and hydrochloric acid, and the solution is examined for a primary aromatic base.

Example.—On odourless solid, decomposes when it is heated, without charring, giving ammonia, and leaves no residue on ignition. It is sparingly soluble in cold water, dissolves in sodium carbonate with effervescence, but is not reprecipitated by acids. It does not give ammonia with damp sodium carbonate (see above). Boiled with caustic soda it gives ammonia. The acid in the alkaline solution is not precipitated on the addition of sulphuric acid, and is non-volatile. Probably a dibasic acid, and is ultimately identified as oxalic acid. But the original compound cannot be oxamide; it might be $\text{NH}_2\cdot\text{CO}\cdot\text{COOH}$, but

¹ See footnote, p. 611. a

as this is a very uncommon substance, it is probably a salt of some very simple basic amide, namely urea.

For the final identification of a solid or liquid a melting-point or boiling-point determination may, of course, be made in many cases, and a liquid may often be converted into some solid derivative of definite melting-point (pp. 137, 138, 407, 453).

Preparations.

PREPARATIONS.

The following are some of the typical compounds for which methods of preparation are described in detail. Many others may be prepared with the aid of the experimental data which are given throughout the book.

- Acetaldehyde, 127.
- Acetamide, 163.
- Acetanilide, 392.
- Acetic anhydride, 161.
- Acetone, 133.
- Acetophenone, 444.
- Acetyl chloride, 159.
- Acetylene, 90.
- Alcohol, 102.
- Allyl alcohol, 230.
- Allyl iodide, 232.
- Aniline, 390.
- Azobenzene, 410.
- Azoxybenzene, 410.
- Benzaldehyde, 438.
- Benzamide, 453.
- Benzenesulphonic acid, 418.
- Benzoin, 441.
- Benzonitrile, 454.
- Benzoquinone, 445.
- Benzoyl chloride, 452.
- Benzoyl derivatives, 452.
- Benzyl alcohol, 436.
- Bromobenzene, 376.
- Carbamide, 240.
- Chlorobenzene, 376.
- Chloroform, 71.
- Cinnamic acid, 463.
- Diazoaminobenzene, 408.
- Diazotisation, 403.
- Diethyl ether, 115.
- Dimethyl ketone, 133.
- m*-Dinitrobenzene, 384.
- Ether, 115.
- Ethyl acetate, 170.
 - " acetoacetate, 181.
 - " alcohol, 102.
 - " benzoate, 451.
 - " bromide, 68.
 - " chloride, 67.
- Ethyl ether, 115.
 - " hydrogen sulphate, 178.
 - " iodide, 68.
 - " malonate, 185.
 - " nitrate, 174.
- Ethylene, 80.
 - " dibromide, 84.
 - " glycol, 215.
- Formic acid, 147.
- Fructose, 288.
- Glucose, 285.
- Grignard reagents, 208.
- Helianthin, 601.
- Hydrazones, 407.
- Iodobenzene, 376.
- Iodoform, 73.
- Maltose, 296.
- Naphthalene- β -sulphonic acid, 486.
- α -Naphthylamine, 483.
- m*-Nitroaniline, 394.
- Nitrobenzene, 383.
- α -Nitronaphthalene, 483.
- Nitrophenols, 426.
- p*-Nitrosodimethylaniline, 397.
- Osazones, 407.
- Oxalic acid, 242.
- Oxamide, 245.
- Oximes, 137.
- Phenyl cyanide, 454.
- Phenyldiazonium chloride, 403.
- Phenylhydrazine, 406.
- Phthalic acid, 458.
- Phthalimide, 458.
- Picric acid, 427.
- Quinoline, 513.
- Quinone, 445.
- Salicylaldehyde, 442.
- Sulphanilic acid, 419.
- Trinitrophenol, 427.
- Urea, 240.

INDEX TO PARTS I. AND II.

Heavy type indicates the more important of two or more references to a compound or subject dealt with in any part of this book.

Pages 1 to 324 are in Part I., pages 325 to 614 in Part II.

- Abel*, 570.
Acenaphthaquinone, 492.
Acenaphthene, 491.
Acetal, 130.
Acetaldehyde, 92, 104, **126**.
Acetaldehyde hydrazone, 138.
Acetaldoxime, 137.
Acetals, 130, 144.
Acetamide, 162.
Acetanilide, 389, **391**.
Acetic acid, **150**, 324.
Acetic acid, electrolysis of, 54.
Acetic acid, salts of, 152, 153.
Acetic anhydride, 161.
Acetic chloride, 159.
Acetoacetic acid, 181, 187.
Acetone, 97, **133**, 323, 324.
Acetone ammonia, 144.
Acetone cyanohydrin, 143.
Acetonedicarboxylic acid, **190**, 261, 535.
Acetone hydrazone, 134, 138.
Acetone mercaptol, 120.
Acetone phenylhydrazone, 134, 138.
Acetone pinacol, 142.
Acetone semicarbazone, 138.
Acetone sodium bisulphite, 134.
Acetonitrile, 163, **317**.
Acetonylacetone, 522.
Acetophenone, 358, **444**.
Acetophenone dichloride, 535.
Acetophenone hydrazone, 407, **444**.
Acetophenoneoxime, 444.
Acetotoluides, 389, **394**.
Acetoxime, 134.
Acetylaminoketones, 544.
Acetylaminophenetole, 427.
Acetylbenzene, 444.
Acetylcellulose, 300.
Acetyl chloride, 159.
Acetylcodeine, 542.
Acetylene, **89**, 95, 324.
Acetylene, polymerisation of, 330.
Acetylene series, **88**, 95.
Acetylene tetrabromide, 92, 495.
Acetylene tetrachloride, **92**, 324.
Acetylformic acid, 191.
Acetylfructose, 289, 307.
Acetylglucose, 286, 307.
Acetyl group, 160, **162**.
Acetylides, 91.
Acetyl-lactic acid, 252.
Acetylmaltose, 297.
Acetylmethylaniline, 397.
Acetylphenetidine, 427.
 β -Acetylpropionic acid, 191.
Acetylsalicylic acid, 471.
Acetylsucrose, 296.
Acetylurea, 556.
Acid amides, 162.
Acid anhydrides, **161**, 247, 458, 503.
Acid bromides, 161.
Acid chlorides, **159**, 452.
Acid dyes, 582.
Acid green, 586.
Acid hydrolysis, 184.
Acid iodides, 161.
Aconitic acid, 261.
Acraldehyde, 232.
Acridine, 596.
Acridine orange R, 597.
Acridine yellow R, 597.
Acridinic acid, 596.
Acridone, 596.
Acriflavine, 596.
Acrolein, 232.
Acrose, 290.
Acrylic acid, **233**, 252.
Active amyl alcohol, **111**, 267, 268, 549.
Acyl radical, 389.
Additive products, 83.
Adenine, 559, **561**.
Adipic acid, **261**, 353.
Adjective dyes, 580.
Adrenaline (Adrenine), 567.
Adrenalone, 567.
Alanine, 203, 251, **548**.
Albumin (blood), 552, **574**.
Albumin (egg), 550, 551, **552**, **573**, 574.
Albumins, 574.

- Albumoses, 572, 575.
 Alcohol, 101, 112, 323, 324.
 Alcohol, absolute, 106.
 Alcohol, constitution of, 47.
 Alcohol, detection of, 104.
 Alcohol, detection of water in, 104.
 Alcohol, determination of, 107.
 Alcoholic fermentation, 102, 302, 303.
 Alcoholic liquors, 304.
 Alcohol, manufacture of, 105.
 Alcoholometry, 107.
 Alcohols, monohydric, 97, 112, 435.
 Alcohols, nomenclature of, 108.
 Alcohols, oxidation of, 109, 115.
 Alcohols, polyhydric, 234, 237, 305.
 Alcohols, trihydric, 219, 237.
 Aldehyde ammonia, 128.
 Aldehyde bisulphite compounds, 128.
 Aldehyde cyanohydrin, 143, 253.
 Aldehyde resin, 128.
 Aldehydes, 122, 139, 437.
 Aldehydes, condensation of, 145.
 Aldehydes, oxidation of, 144.
 Aldehydes, polymerisation of, 125, 129.
 Aldimines, 438, 442.
 Aldohexoses, 305.
 Aldol, 129.
 Aldol condensation, 130.
 Aldopentoses, 305.
 Aldoses, 292, 305.
 Aldotetroses, 305, 306.
 Aldoximes, 137, 317.
Aldrich, 567.
 Algol blue K, 595.
 Aliphatic compounds, 351.
 Alizarin, 498.
 Alizarin blue, 595.
 Alizarin Bordeaux R, 594.
 Alizarin cyanines, 594.
 Alizarin diacetate, 500.
 Alizarin, dyeing with, 580.
 Alizarin green, 595.
 Alkali blue, 590.
 Alkaloids, 526.
 Alkaloids, constitution of, 527.
 Alkaloids, contained in opium, 541.
 Alkaloids, derived from pyridine, 529.
 Alkaloids, derived from quinoline, 537.
 Alkaloids, extraction of, 526.
 Alkaloids, synthetic, 536.
 Alkylamino-acids, 552.
 Alkylanilines, 395.
 Alkyl chlorides, 66, 76.
 Alkyl cyanides, 316.
 Alkyl cyanurates, 322.
 Alkylene dichlorides, 75.
 Alkylene radicals, 75, 78.
 Alkyl glucosides, 306.
 Alkyl halogen compounds, 69, 76.
 Alkyl hydrides, 75.
 Alkyl hydrogen sulphates, 87, 177.
 Alkyl isocyanates, 321.
 Alkyl isocyanides (isonitriles), 317.
 Alkyl isocyanurates, 322.
 Alkyl isothiocyanates, 321.
 Alkyl radicals, 75.
 Alkyl thiocyanates, 321.
 Allelotropic mixtures, 189.
 Allene, 94.
 Allocinnamic acid, 405.
 Alloxan, 556.
 Allyl alcohol, 230, 357.
 Allylaniline, 516.
 Allyl bromide, 232.
 Allyl disulphide, 232.
 Allylene, 94.
 Allyl formate, 230.
 Allyl iodide, 231.
 Allyl isothiocyanate, 232, 320.
 Allyl sulphide, 232.
 Aluminium carbide, 63.
 Aluminium ethyl, 211.
 Aluminium ethoxide, 103, 114, 145.
 Aluminium isopropoxide, 143.
 Amatol, 385.
 Amides, 162.
 Amidol, 433.
 Amines, 192, 211, 399.
 Amines, identification of, 200.
 Amines, preparation of, 198, 211.
 Amines, separation of primary, secondary, and tertiary, 199, 212.
 Aminoacetic acid, 202, 213, 548.
 Amino-acids, 201, 213, 542.
 Amino-acids, benzoyl derivatives of, 545.
 Amino-acids, classification of, 547.
 Amino-acids, esters of, 544.
 Amino-acids, resolution of, 545.
 β -Aminoanthraquinone, 595.
 Aminoazobenzene, 408, 597.
 Aminoazobenzenedisulphonic acid, 602.
 Aminobenzenesulphonamide, 419.

- Aminoazo-compounds, 409.
 Aminoazotoluene hydrochloride, 597.
 Aminobenzaldehydes, 440, 516.
 Aminobenzene, 390.
 Aminobenzenesulphonic acids, 419.
 Aminobenzoic acids, 455, 471, 607.
 Aminobenzoylformic acid, 525.
 Amino-compounds, 386.
 Aminodibromobenzenes, 349.
 Aminodichloropurine, 562.
 β -Aminoethanesulphonic acid, 565.
 Aminoethyl alcohol, 459.
 Aminoethylindole, 552.
 Aminoformic acid, 203.
 Aminoglutaric acid, 550.
 Aminoguanidine, 563.
 β -Amino- β -hydroxypropane, 144.
 Aminoisocaproic acid, 549.
 Aminoisovaleric acid, 549.
 Aminomethylvaleric acid, 549.
 Aminonaphthalene, 476, 483.
 α -Amino- β -naphthol, 487.
 1:4-Aminonaphthol, 487.
 Amino-6-oxypurine, 559, 562.
 Aminophenetole, 427.
 Aminophenol, 388, 414, 421.
 Aminophenylacetic acid, 525.
 Aminophenylaminopropionic acid, 551.
 α -Aminopropionic acid, 203, 548.
 β -Aminopropionic acid, 548.
 Aminopurine, 559, 561.
 β -Aminopyridine, 531.
 Aminosuccinic acid, 255, 550.
 Aminotoluene, 394.
 Aminouracil, 558.
 Amygdalin, 310, 437.
 Amyl acetate, 180.
 Amyl alcohols, 111, 112, 267, 323, 549.
 Amylase, 300, 304.
 Amyl cyanide, 268.
 Amylene, 85, 86.
 Amyl hydrogen sulphate, 111.
 Amyl iodide, 268.
 Amyl-*m*-cresol, 429.
 Amyl nitrite, 175.
 Amylodextrin, 300.
 Amylo-process, 106.
 Amylum, 298.
 Anæsthetics, local, 536.
 Analysis of organic salts, 29.
 Anderson, 505, 520.
 Anethole, 443, 472.
 Anhydrides, 161, 247.
 Aniline, 390.
 Aniline black, 446, 605.
 Aniline blue, 590.
 Aniline, homologues of, 394.
 Aniline, substitution products of, 393.
 Aniline-*p*-sulphonic acid, 419.
 Aniline sulphonic acids, 419.
 Anils, 282.
 Animal charcoal, 6.
 Animal starch, 299.
 Anisaldehyde, 443, 472.
 Aniseed, oil of, 443.
 Anisic acid, 472.
 Anisole, 426.
 Anisyl alcohol, 472.
 Anthracene, 328, 492.
 Anthracene derivatives, isomerism of, 495.
 Anthracene dichloride, 496.
 Anthracene oil, 326, 328.
 Anthracene picrate, 492.
 Anthranilic acid, 455, 470, 607.
 Anthranol, 498.
 Anthrapurpurin, 501.
 Anthraquinone, 496.
 Anthraquinonedisulphonic acid, 498, 501.
 Anthraquinone- β -monosulphonic acid, 498, 499.
 Anthraquinone violet, 594.
 Antifebrin, 392.
 Antimeric compounds, 271.
 Antipyrine, 523.
 Apomorphine, 542.
 Apple oil, 180.
 Arabinose, 235, 306.
 Arabinulose, 307.
 Arabitol, 235.
 Arbutin, 432.
 Arginine, 550.
 Argol, 256.
 Armstrong, 335.
 Aromatic alcohols, 435.
 Aromatic aldehydes, 437.
 Aromatic-aliphatic cyclic compounds, 489.
 Aromatic amines, 399.
 Aromatic compounds, general properties of, 351.
 Aromatic compounds, reduction of, 356.
 Aromatic halogen derivatives, 371.
 Arsenic, derivatives of, 204.

- Arsenic, detection of, 16.
 Arsines, 204.
 Arsonium salts, 205.
 Artificial lacquers, 301.
 Artificial silk, 301, 302.
 Aryl radicals, 365.
 Ascorbic acid, 571.
 Aseptic distillation, 190.
 Aseptol, 429.
 Asparagine, 255, 550.
 Aspartic acid, 255, 550.
 Aspirin, 471.
 Asymmetric carbon atom, 267.
 Atropic acid, 535.
 Atropine, 533.
 Aurichlorides, 195.
 Aurin, 590.
 Auxochrome, 584.
 Azelaic acid, 234, 261.
 Azeotropic mixture, 106.
 Azides, 414.
 Azidoacetic acid, 414.
 Azimido-compounds, 414.
 Azines, 138.
 Azobenzene, 410, 412, 597.
 Azobenzenesulphonic acid, 597.
 Azo-blue, 604.
 Azo-compounds, 408, 597.
 Azo-dyes, 597.
 Azoimide, 414.
 Azotoluene, 411.
 Azoxybenzene, 410, 412.
 Azoxy-compounds, 410.
 Azulmic acid, 309.

Bacterium aceti, 104, 151.
Baeyer, 335, 524, 552, 557, 607.
 Bakelite, 124, 426.
 Ballistite, 301.
Banting, 569.
Barbier, 213.
 Barbituric acid, 556.
Barger, 568.
 Barley-sugar, 295.
 Basic dyes, 582.
Baumann, 568.
Baumann and Schotten's method, 453, 568.
 Bauxite, 64.
Beckmann, 38, 41.
Beckmann transformation, 138.
 Beer, preparation of, 304.
 Beet-sugar, 294.
Behrend, 557.
 Benzal chloride, 379, 438.
 Benzaldehyde, 358, 437.
 Benzaldehyde semicarbazone, 440.
 Benzaldoximes, 439.
 Benzalphenylhydrazone, 439.
 Benzal radical, 379.
 Benzamide, 453.
 Benzamine, 537.
 Benzanilide, 392.
 Benzene, 327 *seq.*, 330.
 Benzeneazobenzene, 404, 600.
 Benzene, constitution of, 333 *seq.*, 348.
 Benzene derivatives, isomerism of, 337.
 Benzene derivatives, orientation of, 343.
 Benzenedicarboxylic acids, 457, 459.
 Benzene-*m*-disulphonic acid, 418.
 Benzene hexabromide, 332.
 Benzene hexacarboxylic acid, 450, 460.
 Benzene hexachloride, 332.
 Benzene, homologues of, 360.
 Benzene picrate, 428.
 Benzene, structure of, 333 *seq.*, 348.
 Benzenesulphonamide, 418.
 Benzenesulphonic acid, 415, 418.
 Benzenesulphonyl chloride, 418, 434.
 Benzidine, 411, 603.
 Benzidine transformation, 411.
 Benzil, 441.
 Benzine, 64.
 Benzoazurine, 604.
 Benzoflavin, 597.
 Benzoic acid, 451.
 Benzoic acid, substitution products of, 454.
 Benzoic anhydride, 452.
 Benzoin, 441.
 Benzoin condensation, 441.
 Benzol, 327, 330.
 Benzolated amylic alcohol, 527.
 Benzonitrile, 453.
 Benzophenone, 445.
 Benzopurpurin, 603, 604.
 Benzopyrrole, 524.
 Benzoquinone *o*-, 447 ; *p*-, 445.
 Benzotoluides, 394.
 Benzotrichloride, 379, 438, 451.
 Benzoylbenzene, 445.
 Benzoylbenzoic acid, 496.
 Benzoyl chloride, 452.
 Benzoyl-derivatives, 452.
 Benzoyllecgonine, 536.
 Benzoylglycine, 202, 451.

- Benzoylmethylaniline, 397.
 Benzoylpiperidine, 510.
 Benzyl acetate, 436.
 Benzyl alcohol, 435.
 Benzylamine, 399.
 Benzyl benzoate, 435.
 Benzyl bromide, 380, 436.
 Benzyl carbinol, 437.
 Benzyl chloride, 378, 436, 438.
 Benzyl cyanide, 454, 462.
 Benzylideneacetone, 440.
 Benzylideneaniline, 440.
 Benzylidene dichloride, 379.
 Benzylidenehydrazone, 407, 439.
 Benzylidenehydroxycyanide, 440.
 β -Benzylidenepropionic acid, 463, 465, 478.
 Benzylidene radical, 379.
 Benzyl iodide, 385.
 Benzylmalonic acid, 462.
 Benzyl radical, 364.
 Benzyltetramethylammonium, 211.
 Beri-beri, 570, 571.
Best, 569.
 Betaine, 553.
 Biebrich scarlet, 602.
 Bis-dehydrothiitoluidine, 606.
 Bis-diazoacetic acid, 413.
 Bismarek brown, 601.
 Bisulphite compounds, 142.
 Biuret, 240.
 Blasting-gelatin, 224, 301.
Blomstrand, 405.
 Blood-albumin, 552, 574.
 Boiling-point, 9.
 Bone-oil, Bone-tar, 505.
 Bordeaux, 602.
 Brilliant green, 586.
 Bromal, 132.
 Bromination, 372.
 Bromination of acids, 165.
 Bromine, detection of, 15.
 Bromine, estimation of, 25.
 Bromoacetic acids, 165.
 Bromoacetylene, 353.
 Bromoanthraquinone, 497.
 Bromobenzene, 374, 376, 398.
 Bromobenzenesulphonic acids, 423.
 Bromobenzoic acids, 454.
 Bromobenzoylbenzoic acid, 497.
 Bromobenzyl bromide, 495, 502.
 Bromobutyric acid, 234, 263.
 Bromochlorobenzene, 373.
 Bromoethane, 68.
 Bromoethylamine, 459.
 Bromoethylene, 84.
 Bromoethylphthalimide, 459.
 Bromoform, 73.
 Bromohydrins, 87.
p-Bromoisopropyl benzene, 369.
 Bromonaphthalenes, 481.
 Bromonitrobenzenes, 385.
 Bromophenanthrene, 503.
 Bromophenyldiazonium chloride, 373.
p-Bromophenylhydrazine, 407.
 Bromophthalic anhydride, 497.
 α -Bromopropionic acid, 251, 252.
 β -Bromopropionic acid, 233, 252.
 Bromopyridine, 505, 521.
 Bromosuccinic acid, 257.
 Bromotoluenes, 378, 455.
 Brucine, 539, 540.
 Brucine methiodide, 540.
Bunsen, 205.
 Butadiene, 95, 111.
 Butaldehyde, 132, 139.
 Butane, 55, 61.
 Butene, 83, 85, 86.
 Butter, 227.
 Butyl acetate, 180.
 Butyl acetone, 184.
 Butyl alcohols, 108, 111, 112, 233.
 Butyl chloral, 132.
 Butylene dibromide, 94.
 Butylene glycol, 87, 219, 236.
 Butylenes, 85, 86, 88.
 Butyl iodide, 68.
 Butyl iodide, secondary, 87.
 Butyl iodide, tertiary, 56.
 Butyric acid, iso, 158, 166.
 Butyric acid, normal, 157, 166.
 Butyrone, 139.
 Butyrophenone, 445.
 Cacodyl, 205.
 Cacodyl chloride, 205.
 Cacodyl cyanide, 205.
 Cacodylic acid, 206.
 Cacodyl oxide, 205.
 Cadaverine, 546.
 Caffeine, 559, 561.
 Calciferol, 566, 571.
 Calcium acetonedicarboxylate, 535.
 Calcium carbide, 89.
 Calcium cyanamide, 319.
 Calico-printing, 582.
 Camphor, 369, 430.
 Cane-sugar, 294.
Cannizzaro's reaction, 436, 440.

- Capraldehyde, 139.
 Capric acid, 168.
 Caproic acid, 158.
 Caramel, 295.
 Carbamic acid, 203.
 Carbamide, 239, 241.
 Carbazole, 504.
 Carbethoxy-derivatives, 239.
 Carbimides, alkyl, 321.
 Carbinol, 108.
 Carbocyclic compounds, 508.
 Carbohydrates, 284, 304.
 Carboic acid, 327, 425.
 Carbon, detection of, 13.
 Carbon, estimation of, 18.
 Carbonic acid, 238, 261.
 Carbon monoxide, products from, 323.
 Carbon suboxide, 246.
 Carbon tetrachloride, 52, 74, 76.
 Carbonyl chloride, 72, 238.
 Carbonyl-group, 135.
 Carbostyryl, 516.
 Carboxyl-group, 155.
 Carboxylic acids, 156, 448.
 Carbylamine reaction, 72, 195, 389.
 Carbylamines, 317.
 Carbyl sulphate, 565.
Carius' method of analysis, 25.
 Carotene, 571.
 Carvacrol, 369, 430.
 Caseinogen (casein), 228, 297, 574, 576.
 Catalytic reduction, 229, 356.
 Catechol, 431, 500.
 Catecholcarboxylic acid, 472.
 Catechu, 431.
 Celanese, 302.
 Cellophane, 302.
 Celluloid, 301.
 Cellulose, 300, 304.
 Cellulose hexa-acetate, 300.
 Cellulose nitrates, 301.
 Celluloses, 284, 304.
 Cellulose xanthates, 302.
 Ceresine, 64.
 Cetyl alcohol, 114.
 Cetyl palmitate, 114.
Chevreul, 553.
 Chloral, 131.
 Chloral alcoholate, 131.
 Chloral hydrate, 131, 164.
 Chloramine T, 419.
 Chloranil, 448.
 Chlorination, 372.
 Chlorination of acids, 165.
 Chlorine carrier, 371.
 Chlorine, detection of, 15.
 Chlorine, estimation of, 25.
 Chloroacetanilide, 393.
 Chloroacetic acid, 164, 324.
 Chloroacetone, 522, 537.
 Chloroacetyl catechol, 567.
 Chloroacetyl chloride, 546, 567.
 Chloroanilines, 393, 414.
 Chloroanthracenes, 496.
 Chlorobenzene, 374, 375.
 Chlorobenzenesulphonic acid, 422.
 Chlorobenzoic acid, 378.
 Chlorobenzyl chloride, 372.
 Chlorocaffeine, 561.
 Chloroethane, 67.
 Chloroethanesulphonic acid, 565.
 Chloroethers, 121.
 Chloroethylene, 84.
 Chloroform, 52, 71, 131.
 Chloroformic acid, 165.
 Chloroformic ester, 238.
 Chloroguanine, 562.
 Chlorohydrins, 87, 218, 222.
 Chloromalonic acid, 254.
 Chloromethane, 66.
 Chloromethyl ether, 189.
 Chloronaphthalenes, 481.
 Chloronitrobenzenes, 375, 385, 393, 422.
 Chlorophenol, 374, 431.
 Chlorophyll, 577.
 Chloropicrin, 73.
 α -Chloropropionic acid, 165, 251.
 β -Chloropropionic acid, 165, 252.
 Chloropyridine, 521.
 α -Chloroquinoline, 516.
 Chlorotoluenes, 378.
 Chloroxylene, 363.
 Cholanic acid, 566.
 Cholesterol, 565.
 Cholic acid, 564, 565.
 Choline, 552.
 Chromogen, 584.
 Chromophore, 583.
 Chrysoidine, 600.
 Cinchomeronic acid, 512.
 Cinchonine, 539.
 Cinchoninic acid, 539.
 Cincho-tannic acid, 538.
 Cinnamic acid, 463.
 Cinnamic aldehyde, 465.
 Cinnamylideneacetic acid, 465.
 Cinnamylidenemalonic acid, 465.

- Cis- and trans-isomerides*, **281**, 465.
 Citric acid, 259.
Citromyces, 259.
Claus, 335.
 Cleaning oil, 64.
Clemmensen reaction, 143, 362.
 Closed-chain compounds, 352.
 Coal-gas, 325.
 Coalite, 326.
 Coal, oxidation of, 450.
 Coal-tar, distillation of, 326.
 Coca, alkaloids of, 535.
 Cocaine, 535.
 Codeine, 541, 542.
 Co-enzyme, 303.
 Coke, 325.
 Collagen, 578.
 Collidines, 510.
 Collodion, 301.
 Colour-base, 585.
 Combustion apparatus, 18, 19.
 Composition of organic compounds, **3**.
 Condensation, **136**, 440, 465.
 Conglomerate, 272.
 Congo corinth, 604.
 Congo dyes, 603.
 Congo red, 603.
 Coniine, 529.
 Constitutional formulæ, 46.
 Constitution of organic compounds, **43**.
 Conyrine, 530.
 Copper acetylide, 91.
 Copper phthalocyanine, 608.
 Coprosterol, 565.
 Cordite, 301.
 Coupling, 410, 597.
 Cracking of petroleum, 65, 323.
 Cream of tartar, 258.
 Creatine, 553.
 Creatinine, 554.
 Creosote oil, 326, 328.
 Cresols, 328, **429**.
 Cresylic acids, 328, 329, 426.
 Cretinism, 568.
 Crotonalcohol, 233.
 Crotonaldehyde, 130, **233**.
 Crotonic acid, 233, **234**, 281, 357.
 Crotonylene, 94.
Crum Brown's rule, 382.
 Cryoscopic method, 37.
 Crystallisation, 5.
 Crystallisation, fractional, 6.
 Crystal violet, 589.
 Cumene, 369.
Curtius, 412, 413.
 Cyamelide, 318.
 Cyanamide, 319, 554.
 Cyanic acid, 318, 321.
 Cyanides, alkyl, 316.
 Cyanides, complex, 314.
 Cyanides, metallic, 312.
 Cyanoacetic acid, 192.
 Cyanobenzamide, 608.
 Cyanobenzyl chloride, 517.
 Cyanobenzyl cyanide, 517.
 Cyanogen, 308.
 Cyanogen chloride, 310, 322.
 Cyanogen compounds, 308.
 Cyanogen iodide, 562.
 Cyanohydrins, **139**, 143, 440.
 Cyanohydrins of mono-saccharides, **291**.
 Cyanotoluene, 454, 517.
 Cyanurates, alkyl, 322.
 Cyanuric acid, 240, 310, 318, 322.
 Cyanuric chloride, 310, 322.
 Cycloheptatriene, 534.
 Cyclohexane, 356, 358, 359.
 Cyclohexanol, 353.
 Cyclohexanone, 353.
 Cymene, 369.
 Cysteine, 548.
 Cystine, 548.
 Daturine, 533.
 Decahydronaphthalene, 358, **482**.
 Decalane, 482.
 Decane, 61.
 Decylic acid (capric acid), 168.
 Deduction of a formula, 27.
 Dehydrothiitoluidine, 606.
 Desiodothyroxine, 568.
 Desmotropic forms, 189.
Dewar, 508.
 Dextrin, 105, **299**, 304.
 Dextrose, 285.
 Dextrotartaric acid, **257**, 275.
Diabetes mellitus, 569.
 Diacetin, 222.
 Diacetoneamine, 136, 537.
 Diacetone alcohol, 136.
 Diacetylenes, 94.
 Diacetylmorphine, 542.
 Diacetylurea, 556.
 Diakon, 234.
 Diallyl, 95.
 Diallyl tetrabromide, 95.
 Dialuric acid, 558.

- Diaminoacridine**, 546.
Diaminoazobenzene, 600.
Diaminobenzenes, 349, 387, 389, 395, 601.
Diaminobenzoic acids, 349.
oo-Diaminobenzophenone, 592.
Diaminocaproic acid, 550.
Diamino-compounds, 387, 389, 395.
Diaminodiphenyl, 411.
oo-Diaminodiphenylmethane, 596.
1:4-Diaminonaphthalene, 487.
1:5-Diaminonaphthalene, 602.
Diaminophenol, 433.
Diaminotriphenylmethane, 586.
Diaminovaieric acid, 550.
Dianisidine, 603, 604.
Diarsenic tetramethyl, 205.
Diastase, 296, 299, 304.
Diazoacetic acid, 412.
Diazo-aliphatic compounds, 412.
Diazoaminobenzene, 408.
Diazoamino-compounds, 408, 414.
Diazoaminomethane, 414.
Diazobenzene chloride, 400.
Diazomethane, 180, 413.
Diazonium compounds, 400.
Diazonium compounds, constitution of, 404.
Diazotisation, 401.
Dibasic acids, 241, 261, 456.
Dibenzopyrone, 592.
Dibenzylamine, 399.
Dibromoaminobenzenes, 349.
Dibromoanthraquinone, 499.
Dibromobenzenes, 347, 376.
Dibromoethane, 71, 143.
Dibromoethylbenzene, 464.
Dibromoethylene, 92.
Dibromohydrindene, 491.
Dibromomalonic acid, 556.
Dibromonitrobenzenes, 349.
Dibromopropane, 84.
Dibromopropionic acid, 234.
Dibromosuccinic acid, 257, 259.
Dicarboxylic acids, 241, 261, 456.
Dicarboxylic acids, electrolysis of, 79, 93, 262.
Dichloroacetic acid, 164.
Dichloroacetone, symmetrical, 237, 260.
Dichloroanthracene, 496.
Dichlorobenzenes, 332, 374, 376, 446.
 $\beta\beta$ -Dichlorodiethyl sulphide, 120.
Dichloroethane, 70, 84, 143.
Dichloroethylenes, 92.
 $\alpha\alpha$ -Dichlorohydrin, 222, 237.
 $\alpha\beta$ -Dichlorohydrin, 237.
Dichloroisoquinoline, 518.
Dichloromethane, 70.
Dichloronaphthalene, 481.
Dichloropentane, 510.
 α -Dichloropropane, 134, 143.
 $\beta\beta$ -Dichloropropionic acid, 165, 237.
Dicyanogen, 308.
Diethoxychloropurine, 560.
Diethyl acetonedicarboxylate, 191.
Diethylamine, 195.
Diethylaniline, 395, 397.
Diethyl carbonate, 73, 239.
Diethylene glycol, 218.
Diethyl ether, 115.
Diethyl ketone, 139, 323.
Diethyl malonate, 185.
Diethylmalonylurea, 556.
Diethylnitrosoamine, 196.
Diethyl oxalate, 245.
Diethylphosphine, 204.
Diethyl sulphate, 179.
Diethyl sulphide, 119.
Diglycerol, 224.
Di-glycollide, 254.
Dihalogen derivatives, 70, 78.
Dihexyl ketone, 139.
Dihydric alcohols, 214, 236.
Dihydric phenols, 420, 422, 430.
Dihydroacridine, 596.
Dihydroanthracene, 495, 496.
Dihydronicotyrine, 532.
Dihydroquinoline, 515.
Dihydroxyacetone, 305.
1:2-Dihydroxyanthraquinone, 498.
1:4-Dihydroxyanthraquinone, 594.
Dihydroxyanthraquinones, 501.
Dihydroxybenzenes, 430.
Dihydroxybenzoic acids, 472.
oo-Dihydroxybenzophenone, 592.
Dihydroxymalonic acid, 556.
Dihydroxynaphthalenes, 487, 488.
Dihydroxyphenanthrene, 503.
Dihydroxyphthalophenone, 591.
Dihydroxystearic acid, 234.
Dihydroxysuccinic acid, 256.
Dihydroxythiophene, 520.
Dihydroxyuracil, 558.
Dihydroxyxanthone, 592.
Di-iodopurine, 560.
Di-isoamyl ether, 120.
Di-isobutyl ether, 120.
Di-isopropyl, 58.

- Di-isopropyl ether, 120.
 Di-isopropyl ketone, 139.
 Diketohydrindenes, 491.
 Diketones, 503, 522.
 Diketopiperazine, 546.
 Dimethoxybenzidine, 603.
 Dimethylacetic acid, 158.
 Dimethylacetylene, 94.
 Dimethylamine, 198.
 Dimethylaminoazobenzene, 409, 597.
 Dimethylaminoazobenzenesulphon-
 ic acid, 601.
 Dimethylaniline, 395, 396, 397.
 Dimethylarsine oxide, 205.
 Dimethylbenzenes, 366.
 Dimethylbenzidine, 411, 603.
 $\beta\gamma$ -Dimethyl- $\beta\gamma$ -butylene glycol, 236.
 Dimethyl carbinol, 108, 110.
 Dimethyl ether, 115, 120.
 Dimethylethylbenzene, 361.
 Dimethylethylenes, 85, 86.
 Dimethylethylmethane, 269.
 Dimethylheptenol, 213.
 Dimethyl ketone, 133.
 Dimethylmalonic acid, 261.
 Dimethyl oxalate, 98, 245.
 Dimethyl-*m*-phenylenediamine, 597.
 Dimethyl-*p*-phenylenediamine, 397, 405, 409, 605.
 Dimethylpiperidonium iodide, 528.
 Dimethylpyridines, 510.
 Dimethylpyrogallol, 433.
 Dimethyl sulphate, 99, 179.
 1:3-Dimethylxanthine, 561.
 3:7-Dimethylxanthine, 559, 560.
 Dinaphthols, 485.
 Dinaphthylsulphone, 486.
 Dinitrobenzenes, 384.
 Dinitromesitylene, 350, 368.
 Dinitro- α -naphthol, 485, 604.
 Dinitro- α -naphtholsulphonic acid, 604.
 Dinitrophenylhydrazine, 407.
 Di-olefines, 94, 96.
 Dioxalin, 230.
 Dioxan, 218.
 Dioxindole, 524, 525.
 Dioxypurine, 559, 560.
 Dipeptides, 546.
 Diphenetidine, 603.
 Diphenic acid, 501, 503.
 Diphenic anhydride, 503.
 Diphenol- γ -pyrone, 592.
 Diphenyl, 370, 501.
 Diphenylamine, 398.
 Diphenyldicarboxylic acid, 501, 503.
 Diphenyl ether, 568.
 Diphenylethylene, 502.
 Diphenylhydrazine, 411.
 Diphenyliodonium hydroxide, 377.
 Diphenyliodonium iodate, 377.
 Diphenyl ketone, 445.
 Diphenylmethane, 370, 445.
 Diphenyl sulphide, 434.
 Diphenyl sulphone, 434.
 Diphenylthiourea, 392.
 Diphenyltolylmethane, 587.
 Diphenylurea, 393.
Dippel's oil, 505.
 Dipropargyl, 95, 333.
 Dipropylamine, 192.
 Dipropyl ether, 120.
 Dipropyl ketone, 139.
 Direct dyes, 580.
 Disaccharides, 294, 304, 307.
 Disacryl, 233.
 Dis-azo-dyes, 598, 602.
 Disodium cyanamide, 212, 319.
 Dissymmetry, 266.
 Distillation, 8.
 Distillation, coal-tar, 326.
 Distillation, fractional, 10, 106.
 Distillation in steam, 7.
 Ditolyl, 502.
Döbner, 516.
 Double bond, 82.
 Dulcitol, 235, 288.
Dumas, 21.
 Dutch liquid, 84.
 Dyes and their application, 578.
 Dynamic isomerism, 189.
 Dynamite, 224.
 Earth-wax, 64.
 Ebullioscopic method, 40.
 Ecgonine, 535, 536.
 Edestin, 549.
 Egg-albumin, 573, 574.
 Elaidic acid, 234, 281.
 Elementary analysis, 12, 17.
 Empirical formula, 29.
 Emulsin, 310, 437.
 Enantiomorphous crystals, 265, 271.
 Enolic forms, 189.
 Enzymes, 102, 303.
 Eosin, 593.
 Epichlorohydrin, 237.
 Epinephrine, 567.

- Ergosterol, 566.
 Erythritol, **235**, 306.
 Erythrose, 306.
 Erythrosin, 593.
 Erythrulose, 307.
 Esterification, 171.
 Esters, 169, 179, 323.
 Esters, identification of, 172.
 Estimation of carbon and hydrogen, 18.
 Estimation of chlorine, bromine, and iodine, 25.
 Estimation of nitrogen, 21.
 Estimation of oxygen, 21.
 Estimation of sulphur and phosphorus, 27.
 Ethaldehyde, 126.
 Ethane, **53**, 61, 92.
 Ethanesulphonic acid, 119.
 Ethanol, 101.
 Ethene, 79.
 Ether, **115**, 120.
 Ethereal salts, 169.
 Ethoxides, 103.
 Ethoxybenzoic acid, 469.
 Ethyl acetate, **169**, 324.
 Ethyl acetoacetate, **181**, 187.
 Ethyl acetoacetate, constitution of, 185, 188.
 Ethyl acetoacetate, hydrolysis of, 183.
 Ethyl acetoacetate, tautomerism of, 188.
 Ethyl acetonedicarboxylate, 191.
 Ethyl acetylacetoacetate, 188.
 Ethyl acetylglycollate, 251.
 Ethyl acetyl-lactate, 252.
 Ethyl acrylate, 357.
 Ethyl alcohol, **101**, 112, 323, 324.
 Ethylamine, 193.
 Ethylamine salts, 195, 428.
 Ethylaniline, 395, 397.
 Ethylates, 103.
 Ethyl azidoacetate, 414.
 Ethylbenzene, 358, 363, **367**.
 Ethyl benzenesulphonate, 417.
 Ethyl benzoate, 451.
 Ethyl benzylacetoacetate, 188.
 Ethylbenzylaniline, 586.
 Ethyl benzylmalonate, 462.
 Ethyl bromide, **68**, 69.
 Ethyl butylacetoacetate, 184.
 Ethyl carbamate, 203.
 Ethyl carbinol, 108.
 Ethyl carbonate, 73, 203, **239**.
 Ethyl carbylamine, 195, **317**.
 Ethyl chloride, **67**, 69.
 Ethyl chloroacetate, 188, 246.
 Ethyl chlorocarbonate, 238.
 Ethyl chloroformate, 238.
 Ethyl citrate, 261.
 Ethyl collidinedicarboxylate, 510.
 Ethyl copper acetoacetate, 182.
 Ethyl cyanide, 317.
 Ethyl cyanoacetate, 192.
 Ethylcyclohexane, 358.
 Ethyl diazoacetate, 412.
 Ethyl dihydrocollidinedicarboxylate, 510.
 Ethyl dipropylacetoacetate, 183.
 Ethylene, **79**, 86.
 Ethylene chlorohydrin, 87, 217, 253, 323.
 Ethylene cyanohydrin, 253.
 Ethylenediamine, 459.
 Ethylene dibromide, 70, 78, **84**.
 Ethylene dichloride, 70, **84**.
 Ethylene dicyanide, 246.
 Ethylenediphthalimide, 459.
 Ethylene glycol, 87, **215**, 236, 323.
 Ethylene oxide, 218, 323.
 Ethylene ozonide, 88.
 Ethylene series, 78, 86.
 Ethyl ether, 115.
 Ethyl ethylacetoacetate, 184.
 Ethylethylene, **85**, 86.
 Ethyl ethylmalonate, 186.
 Ethyl ethylmethylacetoacetate, 183.
 Ethyl ethylpropylacetoacetate, 184.
 Ethyl formate, **148**, 173.
 Ethyl glycollate, 251.
 Ethyl hydrindenedicarboxylate, 490.
 Ethyl hydrogen dithiocarbonate, 239.
 Ethyl hydrogen oxalate, 148.
 Ethyl hydrogen sulphate, 81, 116, **178**.
 Ethyl hydroxycrotonate, 188.
 Ethylidene dibromide, **70**, 143.
 Ethylidene dichloride, 54, 143.
 Ethyl iodide, **68**, 69.
 Ethyl isocyanate, 321.
 Ethyl isonitrile, 317.
 Ethyl lactate, 252.
 Ethyl magnesium bromide, 207.
 Ethyl malonate, **185**, 191.
 Ethylmalonic acid, 261.
 Ethyl mandelate, 474.
 Ethyl mercaptan, 118.
 Ethyl methylacetoacetate, 182.

- Ethyl nitrate, 174.
 Ethyl nitrite, 175.
 Ethyl nitrocinnamate, 464.
 Ethyl oxalacetate, 190.
 Ethyl oxalate, 245.
 Ethyl phosphine, 204.
 Ethyl phthalate, 458.
 Ethyl phthalimide, 459.
 Ethyl propylacetic acid, 184, 187.
 Ethyl propylacetoacetate, 183.
 Ethyl propylethylmalonate, 186.
 Ethyl propylmalonate, 187.
 Ethyl propylmalonic acid, 187.
 Ethylpyridine, 534.
 Ethyl salicylate, 470.
 Ethyl sodioacetoacetate, 182, 188.
 Ethyl sodiomalonate, 186, 191.
 Ethyl succinimide, 262.
 Ethyl sulphate, 179.
 Ethyl sulphide, 119.
 Ethyl sulphone, 119.
 Ethylsulphuric acid, 178.
 Ethyl β -uramidocrotonate, 557.
 α -Eucaïne, 536.
 β -Eucaïne, 537.
 Euflavine, 596.
 Euxanthic acid, 591.
 Euxanthone, 591, 592.
 Evipan, 556.
 Exhaustive methylation, 528.
 External compensation, 272.

Faraday, 330.
 Fats, 224.
 Fats, rancidity of, 228.
 Fatty acids, 146, 166, 225.
 Fatty acids, electrolysis of, 54, 62.
 Fatty acids, synthesis of, from ethyl acetoacetate, 181.
 Fatty acids, synthesis of, from ethyl malonate, 186.
 Fatty compounds, 351.
Fehling's solution, 286.
 Ferment, 102, 302.
 Fermentation, 102, 302.
 Fermentation, acetic, 151.
 Fermentation, alcoholic, 102, 303.
 Fermentation, butyric, 157.
 Fermentation, diastatic, 304.
 Fermentation, lactic, 157.
Fernbach's culture, 111.
 Ferrous potassioferrocyanide, 310.
 Fibroin, 548.
Fischer, 290, 293, 543, 546, 559.
Fittig's reaction, 362.

 Fluoran, 592.
 Fluorescein, 592.
 Fluorescein reaction, 432, 457.
 Formaldehyde, 100, 122, 139.
 Formaldehyde, estimation of, 124.
 Formalin, 123.
 Formamide, 163.
 Formanilide, 392.
 Formic acid, 100, 146, 166.
 Formic acid, salts of, 148.
 Formonitrile, 312.
 Formose, 126, 289.
 Formula, deduction of a, 27.
 Fractional crystallisation, 6.
 Fractional distillation, 10, 106.
Frankland, 62.
 Freezing-point, 37.
Friedel and Crafts' reaction, 361, 382, 444, 480.
 Fructose, 102, 288, 304.
 Fructose oxime, 289.
 Fructose penta-acetate, 289, 307.
 Fructosephenylhydrazone, 290.
 Fuchsine, 588.
 Fulminic acid, 319, 321.
 Fumaric acid, 256, 279.
 Fumaric acid, electrolysis of, 93.
 Furan, 518, 519, 523.
 Furancarboxylic acid, 519.
 Furfural, 519.
 Furfuralcohol, 519.
 Furfuraldehyde, 307, 519.
 Furil, 520.
 Furoin, 519.
 Fusel oil, 106, 110, 111, 303.

 Galactonic acid, 288.
 Galactose, 287, 297, 304.
 Gallic acid, 472.
 Gas liquor, 325.
 Gasoline, 64.
Gattermann, 403, 439, 442.
Gay-Lussac, 34.
 Gelatin, 577.
 Gelignite, 224, 301.
 General formulæ, 60.
 Geometrical isomerism, 281, 283, 465.
Gerhardt, 513.
 Glacial acetic acid, 150.
 Gliadin, 550, 552.
 Globulins, 573, 574.
 Gluconic acid, 287, 307.
 Gluconolactone, 293.
 Glucosates, 286.

- Glucosazone, 290.
 Glucose, 102, **285**, 304, 306.
 Glucose cyanohydrin, 292.
 Glucose oxime, 287.
 Glucose penta-acetate, 286, 307.
 Glucosephenylhydrazone, 290.
 Glucosides, **306**, 310.
 Glucosone, 291.
 Glucuronic acid, 591.
 Glutamic acid, 550.
 Glutardialdehyde, 506.
 Glutaric acid, 261, 262.
 Gluten, 299.
 Glyceraldehyde, 221, 305.
 Glyceric acid, 221.
 Glycerides, 225.
 Glycerin, 220.
 Glycerol, **220**, 225, 226, 237.
 Glycerophosphoric acid, 564.
 Glyceryl acetate, 220, 222.
 Glyceryl bromohydrins, 231.
 Glyceryl chlorohydrin diacetate, 237.
 Glyceryl chlorohydrins, **222**, 231, 237.
 Glyceryl trichloride, 223.
 Glyceryl tri-iodide, 232.
 Glyceryl trinitrate, 223.
 Glycine, **202**, 213, 548.
 Glycine anhydride, 546.
 Glycine hydrochloride, 202.
 Glycocholic acid, 564.
 Glycogen, **299**, 304.
 Glycol, **215**, 236.
 Glycol diacetate, 180, **216**.
 Glycol dinitrate, 217.
 Glycol ethers, 218, 323.
 Glycol, sodium compounds of, 215.
 Glycollic acid, 218, 221, **250**.
 Glycollic aldehyde, 218, 305.
 Glycollide, 254.
 Glycols, **214**, 236.
 Glycylglycine, 546.
 Glyoxal, 218, **219**, 257, 353.
 Glyoxylic acid, 218.
 Glycerol resins, 221, 458.
Gmelin, 565.
 Goitre, 568.
Graebe, 477, 499.
 Granulose, 298.
 Grape-sugar, 285.
 Graphic formulæ, 45.
Griess, 349, 400.
Grignard reagents, **207**, 213, 380.
Groves' process, 66, 67.
 Guaiacol, 431.
 Guanidine, 562.
 Guanine, 559, **562**.
 Gum benzoin, 451.
 Gun-cotton, 301.
 Hæmatein, 576.
 Hæmin, 576.
 Hæmoglobin, 575.
 Halogen carrier, 164, **371**.
 Halogen derivatives, 65, 371.
 Hard soap, 226.
Harington, 568.
 Heavy oil, 326, 328.
 Helianthin, 601.
 Helium, 63.
Hell, 165.
 Hemihedral crystals, 265, 271.
 Hemimellitene, 369.
 Hemlock, alkaloids of, 529.
 Heptaldehyde, **132**, 139.
 Heptane, 61.
 Heptyl alcohol, normal, 132.
 Heptylic acid, 132, **158**, 166, 292.
 Heroin, 542.
 Heterocyclic compounds, 507.
 Hexa-acetyl cellulose, 300.
 Hexacarboxybenzene, 337, **460**.
 Hexachloroethane, 54.
 Hexa-ethylene glycol, 218.
 Hexahydric alcohols, **235**, 237, 305.
 Hexahydrobenzene, 332, 356, 358.
 Hexahydropyridine, 505, **509**.
 Hexahydrotetrahydroxybenzoic acid, 538.
 Hexamethylbenzene, 460.
 Hexamethylene, 356, 358.
 Hexamethylenetetramine, 124.
 Hexamethylpararosaniline, 589.
 Hexamine, 124.
 Hexane, 58, 61.
 Hexitols, **235**, 305.
 Hexoses, 305.
 Hexyl alcohol, 235.
 Hexyl chloride, 113.
 Hexylene, 86.
 Hexylic acids, 158.
 Hexyl iodide, 235, 292.
 Hippuric acid, 202, 451.
 Histidine, 551.
Hofmann's bromoamide reaction, 193.
Hofmann's carbylamine reaction, 72, 195.

- Hofmann's* vapour density apparatus, 34.
- Homocyclic compounds, 507.
- Homologous series, 59.
- Homologous series, ascent of, 200.
- Homologous series, descent of, 168, 200.
- Homophthalic acid, 517.
- Homophthalimide, 517.
- Hopkins*, 570.
- Hormones, 566.
- Hydracrylic acid, 252.
- Hydraziaetic acid, 413.
- Hydrazines, 405.
- Hydrazobenzene, 411, 412.
- Hydrazoic acid, 414.
- Hydrazones, 138, 290.
- Hydrindamine, 491.
- Hydrindene, 490.
- Hydrindenecarboxylic acid, 491.
- Hydrindone, 490, 491.
- Hydrobenzamide, 440.
- Hydrobenzoin, 441.
- Hydrocarbons, 49, 78, 88, 360.
- Hydrocarbons, aromatic, oxidation of, 449.
- Hydrocarbons, saturated, 49.
- Hydrocarbons, unsaturated, 78, 88.
- Hydrocinnamic acid, 462.
- Hydrogen cyanide, 310, 320.
- Hydrogen, detection of, 14.
- Hydrogen, estimation of, 18.
- Hydrolysis, 169, 171, 172, 180.
- Hydroquinone, 431, 432, 446.
- Hydroxides, quaternary ammonium, 197.
- Hydroxides, quaternary arsonium, 205.
- Hydroxides, quaternary phosphonium, 204.
- Hydroximes, 136, 199.
- Hydroxyacetic acid, 250.
- Hydroxy-acids, 249, 254, 263, 466.
- Hydroxyaldehydes, aromatic, 441.
- Hydroxyalkyl sulphites, 142.
- Hydroxyaminobenzoic acid, 349.
- Hydroxyaminonaphthalenes, 480.
- β -Hydroxy- α -aminopropionic acid, 548.
- Hydroxyanthraquinones, 497, 498, 499, 501, 594.
- Hydroxyazobenzene, 597.
- Hydroxyazo-compounds, 410, 600.
- Hydroxybenzaldehydes, 442, 443.
- Hydroxybenzene, 425.
- Hydroxybenzoic acids, 351, 466 *seq.*, 471.
- Hydroxybenzyl alcohols, 471, 472.
- α -Hydroxybutyric acid, 263.
- β -Hydroxybutyric acid, 188, 234, 263.
- γ -Hydroxybutyric acid, 263.
- Hydroxycarboxylic acids, 249, 263, 466.
- Hydroxycyanides, 139, 143, 440.
- Hydroxydicarboxylic acids, 254, 264.
- Hydroxyethanesulphonic acid, 565.
- Hydroxy-ethers, 224.
- Hydroxyethyl cyanide, 143.
- Hydroxyethyltrimethylammonium hydroxide, 552.
- Hydroxyformic acid, 249.
- Hydroxyglutamic acid, 551.
- Hydroxyindole, 525.
- Hydroxyisobutyric acids, 263.
- Hydroxyisopropyl cyanide, 143.
- Hydroxylamine, 137, 174.
- Hydroxymalonic acid, 254.
- Hydroxymonocarboxylic acids, 249, 263.
- Hydroxynaphthalenes, 484.
- Hydroxyphenylaminopropionic acid, 551.
- Hydroxyphenylethylamine, 551.
- Hydroxyproline, 552.
- α -Hydroxypropionic acid, 250, 251.
- β -Hydroxypropionic acid, 250, 252.
- Hydroxyquinol, 432, 434.
- 2-Hydroxyquinoline, 516.
- Hydroxysuccinic acid, 254.
- Hydroxysulphites, 142.
- Hydroxysulphonic acids, 429.
- Hydroxytoluenes, 429.
- Hydroxytricarboxylic acids, 259.
- Hydroxyuracil, 558.
- γ -Hydroxyvaleric acid, 191, 263.
- Hyoscyamine, 533.
- Hypnone, 444.
- Hypoxanthine, 559, 560.
- Ice-colours, 599.
- Identification of organic compounds, 12, 13, 609.
- Imides, 249, 262, 458, 556.
- Iminourea, 562.
- Indanthrene blue R, 595.
- Indene, 490, 491.
- Indene dibromide, 491.
- Indian yellow, 591.

- Indican, 606.
 Indigo (indigotin), 441, 466, 525, 582, **606**.
 Indigo-blue, 582, **606**.
 Indigo-carmine, 607.
 Indigodisulphonic acid, 606.
 Indigo, dyeing with, 582.
 Indigo, synthesis of, 441, 466, 607.
 Indigo-white, 524, 582, 606.
 Indirect dyes, 580.
 Indole, 524.
 β -Indole- α -aminopropionic acid, 552.
 Indole- α -carboxylic acid, 525.
 Indophenin reaction, **330**, 365, 520.
 Indoxyl, 524, **525**, 606, 608.
 Indoxyllic acid, 608.
 Ingrain dyes, 599.
 Insulin, 569.
 Internal compensation, 274.
 Inulin, 288, 304.
 Inversion, **296**, 303.
 Invertase, 303.
 Invert sugar, 296.
 Iodine, as a catalyst, 114, 164, 371.
 Iodine, detection of, 15.
 Iodine, estimation of, 25.
 Iodine value, of a fat, 229.
 Iodoacetic acids, 165.
 Iodobenzene, 374, **376**, 398.
 Iodobenzene dichloride, 377.
 Iodoethane, 68.
 Iodoform, **73**, 76.
 Iodoform reaction, 104.
 Iodonitrobenzenes, 385.
 Iodosobenzene, 377.
 Iodotoluenes, 378.
 Iodoxybenzene, 377.
 Ionamines, 599.
Ipatiew, 229.
 Isæthionic acid, 565.
 Isatin, 524, **525**.
 Isatin chloride, 525.
 Iso-alcohols, 109.
 Isoamyl alcohol, **111**, **112**.
 Isoamylamine, 549.
 β -Isoamylene, 85.
 Isoamyl isovalerate, 180.
 Isobutaldehyde, 139.
 Isobutane, 56, 58.
 Isobutyl alcohol, **108**, **111**, **112**.
 Isobutyl carbinol, **111**, 549.
 Isobutylene, **85**, 110.
 Isobutyric acid, **158**, 166.
 Isobutyryne, 139.
 Isocapro lactone, 288.
 Isocrotonic acid, **234**, 281.
 Isocyanates, alkyl, 321.
 Isocyanides, 77, 317.
 Isocyanurates, alkyl, 322.
 Isocyanuric acid, 322.
 Iso-hydrocarbons, 58.
 Isoleucine, 549.
 Isomeric change, 239.
 Isomerism, 58.
 Isomerism, geometrical, 281.
 Isomerism, optical, 271.
 Isonicotinic acid, 511, 512.
 Isonitriles, 77, 317.
 Isopentane, 58.
 Isophthalic acid, **345**, **459**.
 Isoprene, 94.
 Isopropylacetic acid, 156, **158**.
 Isopropyl alcohol, **110**, **112**, 133.
 Isopropylamine, 211.
 Isopropylbenzene, 369.
 Isopropyl bromide, 87.
 Isopropyl carbinol, 108, **111**.
 Isopropyl iodide, **70**, 232.
 Isopropylmethylbenzene, 369.
 Isoquinoline, 504, **517**.
 Isoquinoline methiodide, 517.
 Isosuccinic acid, 249.
 Isothiocyanates, alkyl, 321.
 Iso-urea, 241.
 Isovaleraldehyde, **139**, 549.
 Isovaleric acid, **156**, **158**, 166, 549.

Journiaux, 40.

Kekulé, 79, 334.
Kendall, 568.
 Keratin, 548.
 Kerosene, 64.
 Keto-forms, 189.
 Ketones, **132**, 139, 443.
 Ketones, condensation of, 135, 145.
 Ketones, oxidation of, 144.
 Ketonic acids, 187, 190, 191.
 Ketonic hydrolysis, 183.
 Ketoses, 292, 307.
 Ketotetroses, 306.
 Ketoximes, 137.
 Kieselguhr, 224.
Kilian, 291.
Kjeldahl's method, **25**.
Knorr, 190.
Kolbe, 54, 62, 467.
Körner, 507.
Körner's orientation method, 346.
Kraft, 168.

- Labile forms**, 189.
Lacquers, artificial, 301.
Lactam group, 516, 525, 557.
Lactic acid, **261**, 267, 271, 548.
Lactide, 254.
Lactides, **254**, 263.
Lactim group, 516, 524, 557.
Lactones, 263, 292.
Lactosazone, 297.
Lactose, 157, **297**, 304.
Lactyl-lactic acid, 254.
Ladenburg, 335, 350, 509, 530.
Lævotartaric acid, 275.
Lævulic acid, **191**, 296.
Lævulose, 288.
Lakes, 500, 582.
Landsberger, 42.
Lanoline, 565.
Lard, 224.
Laudanum, 541.
Lauric acid, 166.
Laurone, 141.
Lavoisier, 1.
Lead phthalocyanine, 609.
Lead tetraethyl, 211.
Le Bel and van't Hoff's theory, 267.
Lecithin, 563.
Leucine, 549.
Leuco-base, 584.
Leuco-compound, 582.
Leuco-malachite green, 585.
Leuco-pararosaniline, 587.
Leuco-rostaniline, 587.
Lewisite, 206, 324.
Lieber's iodoform reaction, 104.
Liebermann, 499.
Liebermann's reaction, 196, 424.
Liebig, 551, 552.
Light oil, **326**, 504.
Light petroleum, 64, 85.
Ligroin, 64.
Linolic acid, 228.
Lipase, 227.
Lubricating oils, 64.
Lutidines, 510.
Lycine, 553.
Lyddite, 428.
Lysine, 550.
Lysol, 429.

Magenta, 588.
Magnesium alkyl halides, **207**, 213.
Magnesium alkyl oxides, 106, 114.
Magnesium benzyl chloride, 380.
Magnesium ethoxide, 106.

Magnesium ethyl bromide, 207.
Magnesium ethyl iodide, 208.
Magnesium methyl iodide, 208.
Magnesium phenyl bromide, 380.
Magnesium propyl bromide, 208.
Malachite green, 585.
Maleic acid, **256**, 279, 353.
Maleic anhydride, 256, 279.
Malic acid, **254**, 268, 271.
Malonic acid, 185, **245**.
Malonylurea, 556.
Malt, 304.
Maltase, 303.
Maltodextrin, 300.
Maltosazone, 297.
Maltose, 105, **296**, 299, 304.
M and B 693, 419.
Mandelic acid, 466, **473**.
Mandelonitrile, 440, 473.
Mannitol, **235**, 287, 289.
Mannoheptose, 293.
Mannonic acid, 287.
Mannonolactone, 293.
Mannononose, 293.
Manno-octose, 293.
Mannosaccharic acid, 288.
Mannose, **287**, 304.
Margaric acid, 159, 169.
Margarine, 228.
Marsh-gas, 49.
Mauveine (mauve), 578, **604**.
Meconic acid, 541.
Medicus, 557.
Melinite, 428.
Melissyl alcohol, 114.
Mellitic acid, 460.
Melting point, 12.
Mercaptans, **118**, 434.
Mercaptides, 119.
Mercaptoles, 120.
Mercuric fulminate, 319.
Mercuric mercaptide, 119.
Mercury, organic compounds of, 210, 213.
Mesitylene, 345, 350, 353, **368**.
Mesitylenic acid, 345, 368.
Mesityl oxide, **136**, 324.
Mesotartaric acid, 257, **276**.
Mesoxalic acid, 556.
Mesoxalylurea, 555, **556**.
Metachloral, 131.
Meta-compounds, 340.
Metaldhyde, 130.
Metals, detection of, 17.
Metals, organic derivatives of, 207.

- Metamerism, 121.
 Metanilic acid, 419.
 Methaldehyde, 122.
 Methane, 49, 61.
 Methane series, 49, 61.
 Methanol, 97.
 Methionine, 549.
 Methoxides, 98.
 Methoxybenzaldehyde, 443.
 Methoxybenzoic acids, 430, 471, 472.
 Methoxybenzyl alcohol, 472.
 Methoxycinchonine, 539.
 Methoxy-group, 528.
 p-Methoxyphenol, 568.
 6-Methoxyquinoline-4-carboxylic acid, 538.
 Methylacetamide, 138.
 Methylacetanilide, 397.
 Methyl acetate, 170.
 Methylacetylene, 94.
 Methylacridone, 596.
 Methylacridonium iodide, 596.
 Methylal, 126.
 Methyl alcohol, 97, 122.
 Methylamine, 198.
 Methylaminophenol, 433.
 Methylaniline, 396.
 Methylated spirit, 107.
 Methylates, 98.
 Methylation, 179, 212, 413.
 Methylation, exhaustive, 528.
 Methyl azide, 414.
 Methylbenzanilide, 397.
 Methylbenzene, 360, 365.
 Methyl benzoate, 452.
 Methyl bromide, 66, 69.
 Methylbutadiene, 94, 529.
 Methylbutylacetic acid, 292.
 Methylbutylmalonylthiourea, 556.
 Methyl butyrate, 180.
 Methyl carbinol, 101.
 Methylcatechol, 431.
 Methyl chloride, 52, 66, 69.
 Methylcinnamic acids, 463, 464.
 Methyleresols, 430.
 Methyl cyanide, 317.
 Methylcyclohexenylmalonylurea, 556.
 Methyl dimethylaminoacetate, 553.
 Methyleneaminoacetonitrile, 213.
 Methyleneaniline, 395.
 Methylene blue, 605.
 Methylene dichloride, 70.
 Methylene di-iodide, 413, 521, 533.
 Methylene glycol, 125, 215.
 Methylenitan, 289.
 Methyl ether, 115.
 Methyl o-ethoxybenzoate, 469.
 Methylenehydrazine, 211.
 Methylenehydrazine, 342, 361.
 Methylenehydrazine, 109, 111, 112, 282, 323.
 Methylenehydrazine, 120.
 Methylenehydrazine, 139, 141, 323.
 Methyl ethylsalicylate, 469.
 Methylglucosides, 306.
 Methylglycine, 552.
 Methylheptenone, 213.
 Methylhydrazine, 413.
 Methyl hydrogen sulphate, 99, 179.
 Methylindole, 524.
 Methyl iodide, 66, 69.
 Methyl isonitrile, 317.
 Methyl isophthalate, 459.
 Methylisopropylbenzene, 369.
 Methylisopropyl ether, 120.
 Methylisopropyl ketone, 140.
 Methylisoquinolinium iodide, 517.
 Methylmalonic acid, 249.
 Methyl o-methoxybenzoate, 471.
 Methyl α -methylacrylate, 234.
 Methylmorphine, 542.
 Methylnaphthalenes, 480.
 Methyl nitrate, 174.
 Methyl nitrite, 175.
 Methyl orange, 601.
 Methyl oxalate, 98, 245.
 Methylphenylnitrosoamine, 397.
 Methylphosphine, 204.
 Methylpiperidine, 509, 528.
 Methyl propionate, 173.
 Methylpropyl ether, 120.
 Methylpropyl ketone, 140.
 Methylpyridines, 508, 510.
 Methylpyridinium iodide, 506.
 Methylpyrrolidine, 531.
 Methylpyrrolidone, 532.
 Methylquinolines, 514, 515.
 Methylquinolinium iodide, 514.
 Methyl salicylate, 469, 470.
 Methylsuccinic acid, 261.
 Methyl sulphate, 99, 179.
 Methyl terephthalate, 460.
 Methylthiobromine, 561.
 Methylthiophene, 520.
 Methyl-p-toluidine, 396.
 Methyltriphenylmethane, 587.
 Methyluracil, 557.

- Methylurethane, 203, 413.
 Methyluric acids, 559.
 Methyl violet, 589.
 Motol, 433.
Meyer, Victor, 35, 520.
Michler's ketone, 589.
 Micro-analysis, 27.
 Middle oil, 326, 327.
 Milk-sugar, 297.
Miller, 516.
Millon's reagent, 575.
 Mineral naphtha, 63.
 Mirror-images, 271.
 Mixed anhydrides, 162.
 Mixed ethers, 121.
 Mixed ketones, 139.
 Molasses, 105, 295.
 Molecular formula, 29.
 Molecular formula, by explosion, 32.
 Molecular rotation, 284.
 Molecular weight, determination of, 32.
 Monastral Fast Blue, 609.
 Monastral Fast Green, 609.
 Monoacetin, 222.
 Monobromopyridine, 505.
 Monocarboxylic acids, 146, 156, 448, 460.
 Monochloroanthracene, 496.
 Monoformin, 147.
 Monogenetic dyes, 581.
 Monohydric alcohols, 97, 112.
 Monohydric phenols, 425.
 Monohydroxynaphthalenes, 484.
 Mono-oxalin, 147.
 Monosaccharides, 285, 304.
 Mordants, 580.
 Morphine, 541.
 Morphine methiodide, 541.
 Mucic acid, 288, 519.
 Murexide reaction, 555.
 Muscarine, 553.
 Mustard-gas, 120.
 Mustard-oil, 320.
 Mustard-oils, 321.
 Myrbane, essence of, 383.
 Myristic acid, 166.
 Myrosin, 320.
 Myxœdema, 568.
 Naphtha, crude, 326.
 Naphthalene, 327, 328, 475.
 Naphthalene, amino-derivatives of, 483.
 Naphthalene, constitution of, 475.
 Naphthalene, derivatives of, 480, 488.
 Naphthalene derivatives, isomerism of, 478.
 1:8-Naphthalenedicarboxylic acid, 492.
 Naphthalenodisulphonic acids, 486.
 Naphthalene green V, 586.
 Naphthalene, homologues of, 480.
 Naphthalene, nitro-derivatives of, 482.
 Naphthalene, orientation of derivatives of, 488.
 Naphthalene picrate, 475.
 Naphthalenesulphonic acids, 485.
 Naphthalene tetrachloride, 481.
 Naphthalic acid, 492.
 Naphthalic anhydride, 492.
 α -Naphthaquinone, 486.
amphi-Naphthaquinone, 488.
 β -Naphthaquinone, 487.
 β -Naphthaquinone hydrazone, 600.
 Naphtha, solvent, 327.
 Naphthionic acid, 486, 602, 603.
 α -Naphthol, 478, 483, 485.
 β -Naphthol, 484, 485.
 α -Naphtholdisulphonic acid, 604.
 β -Naphtholdisulphonic acid, 602.
 α -Naphtholmonosulphonic acid, 604.
 Naphtholmonosulphonic acids, 486.
 α -Naphtholtrisulphonic acid, 604.
 Naphthol yellow, 485, 604.
 Naphthol yellow S, 604.
 α -Naphthylamine, 476, 483, 484, 489.
 β -Naphthylamine, 484.
 Naphthylaminemonosulphonic acids, 486.
 1:4-Naphthylaminesulphonic acid, 486.
 Narcotine, 541.
 Natural gas, 63.
 Neurine, 553.
 Nickel, as a catalyst, 229, 357, 359.
 Nickel oxide, as a catalyst, 229.
 Nicotine, 530.
 Nicotine dimethiodide, 531.
 Nicotinic acid, 505, 511, 512, 531.
 Nicotyrine, 531.
 Nightshade, alkaloids of, 533.
 Ninhydrin, 491, 544, 575.
 Nitrates, alkyl, 173.
 Nitrates, cellulose, 301.
 Nitration, 380.

- Nitriles, 316.
 Nitrites, alkyl, 175.
 Nitroacetanilides, 393.
 Nitroalizarin, 501, 595.
 Nitroaminomesitylene, 350.
p-Nitroaniline red, 599.
 Nitroanilines, 388, 393 *seq.*, 599.
o-Nitroanisole, 603.
 γ -Nitroanthracene, 493.
p-Nitroazobenzenes, 409.
 Nitrobenzaldehydes, 440.
 Nitrobenzene, 383.
 Nitrobenzene, reduction of, 412.
 Nitrobenzenesulphonic acids, 419.
 Nitrobenzoic acids, 455.
o-Nitrobenzoyl chloride, 525.
p-Nitrobenzoyl chloride, 453.
 Nitrobromobenzenes, 385.
 Nitrochlorobenzenes, 385.
 Nitrochloroform, 73.
 Nitrocinnamic acids, 440, 464.
 Nitro-compounds, 175, 354, 380.
 Nitrodibromobenzenes, 349.
 Nitroethane, 175.
 Nitrogen, detection of, 14.
 Nitrogen, estimation of, 21.
 Nitrogen, optically active compounds of, 282.
 Nitroglycerin, 223.
 Nitroguanidine, 562.
 Nitrohexane, 62.
 Nitrohydroxybenzene, 338.
 Nitriodobenzenes, 385.
 Nitrolic acids, 177.
 Nitrolim, 319.
 Nitromesidine, 350.
 Nitromesitylene, 368.
 Nitrometer, *Schiff's*, 23.
 Nitromethane, 177.
 α -Nitronaphthalene, 476, 482, 488.
 β -Nitronaphthalene, 483.
 β -Nitro- α -naphthylamine, 483.
 Nitroparaffins, 62, 175, 181.
o-Nitrophenetole, 603.
 Nitrophenols, 426.
o-Nitrophenylacetic acid, 525.
 Nitrophenylaminopropionic acid, 551.
p-Nitrophenyldiazonium chloride, 602.
 Nitrophenyldibromopropionic acids, 464, 466.
p-Nitrophenylhydrazine, 407.
 Nitrophenylpropionic acid, 466.
 Nitrophthalic acid, 476.
 Nitrosamine red, 602.
 Nitrosoamines, 196, 212, 396.
 Nitrosobenzene, 411, 412.
 Nitrosodimethylaniline, 397, 605.
 Nitrosomethylurea, 413.
 Nitrosomethylurethane, 413.
 Nitrosophenol, 397, 424, 446.
 Nitrosopiperidine, 509.
 Nitrothiophene, 523.
 Nitrotoluenes, 385, 455, 603.
 Nitrouracil, 557.
 Nitrouracilic acid, 557.
 Nitrourea, 241.
 Nitroxyene, 363.
 Nonane, 61.
 Nonylic acid, 234.
 Normal alcohols, 109.
 Normal hydrocarbons, 58.
 Novocaine, 537.
 Nux vomica, alkaloids of, 539.
 Octa-acetylmaltose, 297.
 Octa-acetylsucrose, 296.
 Octadecapeptide, 547.
 Octane, 61, 530.
 Octyl cyanide, 317.
Enanthal, 132, 139.
Enanthone, 139.
 Oil of aniseed, 443.
 Oil of bitter almonds, 437.
 Oil of mustard, 232.
 Oil of turpentine, 369.
 Oil of wintergreen, 97, 469.
 Oils, 224.
 Oils, drying of, 230.
 Oils, hardening of, 228.
 Olefiant gas, 79.
 Olefines, 78, 86.
 Olefines, additive reactions of, 86 *seq.*
 Olefinic acids, 233, 237, 463.
 Oleic acid, 225, 228, 234, 281.
 Olein, 227.
 Open-chain compounds, 352.
 Opium, 541.
 Optical isomerism, 265, 271, 281.
 Optically active nitrogen compounds, 282.
 Optically active substances, 265.
 Organic acids, esters of, 169.
 Organic compounds, classification of, 351.
 Organo-metallic compounds, 207.
 Orientation of aromatic compounds, 343.

- Orientation rules, 382.
 Ornithine, 550.
 Ortho-compounds, 340.
 Orthoquinones, 447, 487, 503.
 Osazones, 290, 407.
 Osones, 291.
 Oxalacetic acid, 190.
 Oxalic acid, 218, **242**, 262.
 Oxalic acid, salts of, 244.
 Oxaluric acid, 555.
 Oxalyl chloride, 245.
 Oxalylurea, 555.
 Oxamide, 245.
 Oxamines, 204.
 Oxanilide, 392.
 Oxanthranol, 498.
 Oxidising agents, 100.
 Oximes, **136**, 199.
 Oxindole, 524, **525**.
 6-Oxydichloropurine, 562.
 Oxygen, estimation of, 21.
 Oxyhamoglobin, 575, **576**.
 Oxyneurine, 553.
 Oxypurine, 559, **560**.
 Ozokerite, 61, **64**.
 Ozonides, **88**, 96.

 Palmitic acid, **158**, 166.
 Palmitone, 139.
 Papaverine, 541.
 Parabanic acid, 555.
 Paracetaldehyde, **130**, 145.
 Para-compounds, 340.
 Paracyanogen, 309.
 Paraffins, 49, **59**, 64.
 Paraffin-wax, 64.
 Paraformaldehyde, 125.
 Paraglyoxal, 219.
 Paralactic acid, 252.
 Paraldehyde, **130**, 145.
 Paranitroaniline red, 602.
 Paraquinones, 445, 486, 496.
 Para-red, 599, **602**.
 Pararosanine, 587.
 Parchment paper, 300.
 Partially racemic salts, 282.
 Passing down a homologous series, 168, 200.
 Passing up a homologous series, 200.
Pasteur, 265, 279.
 Pear oil, 180.
 Pelargonic acid, 234.
 Penta-acetylfructose, 289, 307.
 Penta-acetylglucose, **286**, 307.
 Pentaerythritol, 145.
 Pentahydric alcohols, **235**, 237, 305.
 Pentamethylbenzene, 337.
 Pentamethylenediamine, 509, **546**, 550.
 Pentamethylpararosanine, 589.
 Pentane, **58**, 61.
 Pentene, 86.
 Pentitols, **235**, 237, 305.
 Pentoses, 306.
 Pentothal, 556.
 Pentylene, 85.
 Pentylenedimethylamine, 528.
 Pepper, alkaloid of, 532.
 Pepsin, 547, 572, 575.
 Peptones, 572, **575**.
 Peracetic acid, 127.
 Peri-position, **480**, 492.
Perkin, 578.
Perkin reaction, **463**, 533.
 Perspex, 234.
 Peru balsam, 451.
 Petroleum, 63.
 Petroleum, cracking of, 65, 323.
 Petroleum ether, 64.
 Phenacetin, 427.
 Phenanthraquinone, 503.
 Phenanthraquinone dioxime, 503.
 Phenanthrene, 328, 492, **501**.
 Phenanthrenecarboxylic acid, 502.
 Phenanthrene dibromide, 503.
 Phenanthrene picrate, 493, 501.
 Phenazone, 523.
 Phenetidine, 427.
 Phenetole, 426.
 Phenol, 327, 328, **425**.
 Phenolic acids, 466.
 Phenolic aldehydes, 441.
 Phenolphthalein, 591.
 Phenols, 420.
 Phenolsulphonic acids, 419, 428, **429**.
 Phenopyrrole, 524.
 Phenylacetaldehyde, 437, **462**, 551.
 Phenyl acetate, 426.
 Phenylacetic acid, 460, **462**.
 Phenylacetoneitrilo, 454, **462**.
 Phenylacetylene, 465.
 Phenylacrylic acid, 461, **463**.
 Phenylalanine, 551.
 Phenylamine, 390.
 Phenylaminoacetic acid, 607.
 Phenyl-*o*-aminobenzoic acid, 596.
 Phenylaminopropionic acid, 551.
 Phenylanthranilic acid, 596.
 Phenyl azide (phenylazoisimide), 414

- Phenyl benzoate, 452.
 Phenyl bromide, 376.
β-Phenyl-*β*-bromopropionic acid, 464.
 Phenylbutylene, 449, 478.
 Phenylbutylene dibromide, 478.
 Phenylbutyric acid, 461.
 Phenyl carbimide, 321, 393.
 Phenyl carbinol, 435.
 Phenylcarbylamine, 72, 391.
 Phenyl chloride, 375.
 Phenylchloroform, 379.
 Phenyl cyanide, 453.
 Phenyldiazonium chloride, 400.
 Phenyldiazonium hydroxide, 400, 405.
 Phenyldiazonium sulphate, 400, 403.
β-Phenyl-*αβ*-dibromopropionic acid, 464, 465.
 Phenyldimethyl carbinol, 437.
 Phenyldimethylpyrazolone, 523.
 Phenylenediacetic acid, 491.
 Phenylenediamines, 349, 387, 389, 395, 601, 602.
 Phenylene radical, 364, 424.
 Phenylethane, 367.
 Phenylethyl alcohol, 437, 462.
 Phenylethyl carbinol, 437.
 Phenylethylene, 464.
 Phenylethyl ether, 426.
 Phenylformic acid, 461.
 Phenylglycine, 607.
 Phenylglycine-*o*-carboxylic acid, 525, 607.
 Phenyl glycollic acid, 473.
 Phenyl group, 364, 424.
 Phenylhydrazine, 405.
 Phenylhydrazones, 138, 290, 407.
 Phenylhydroxylamine, 411.
 Phenyl iodide, 376.
 Phenyl isocyanate, 321.
 Phenyl isocyanide, 72.
 Phenyl isothiocyanate, 392.
 Phenyl-lactic acid, nitrile of, 551.
 Phenyl mercaptan, 434.
 Phenylmethane, 365.
 Phenylmethylacrylic acid, 463.
 Phenylmethylamine, 396.
 Phenylmethyl carbinol, 444.
 Phenylmethyl ether, 426.
 Phenylmethyl ketone, 444.
 Phenylmethylnitrosoamine, 397.
 Phenylmethylpyrazolone, 523.
 Phenyl mustard oil, 392.
 Phenylnitromethane, 385.
 Phenylnitrosohydroxylamine, 411.
 Phenylpropionic acid, 461, 465.
 Phenylpropionic acid, 449, 461, 462.
 Phenylpropionyl chloride, 491.
 Phenyl radical, 364, 424.
 Phenyl salicylate, 471.
 Phenyl thiourethanes, 392.
 Phenyltolyl ether, 568.
 Phenyltrimethylammonium iodide, 389.
 Phenyl urethanes, 393.
 Phloroglucinol, 385, 432, 433.
 Phloroglucinol triacetate, 434.
 Phloroglucinol trioxime, 434.
 Phorone, 136.
 Phosgene, 72, 238.
 Phosphines, 204.
 Phospho-proteins, 575.
 Phosphorus, detection of, 16.
 Phosphorus, estimation of, 27.
 Photogene, 64.
 Phthaleins, 590.
 Phthalic acid, 457, 476.
 Phthalic acids, 344, 456.
 Phthalic anhydride, 458, 496, 607.
 Phthalimide, 455, 458, 607.
 Phthalocyanines, 608.
 Phthalophenone, 590.
 Phthalyl chloride, 458.
 Physical isomerides, 271.
 Phytosterols, 566.
 Picolines, 510, 511.
 Picolinic acid, 511, 512.
 Picric acid, 427, 579.
 Pictet, 531.
 Pimelic acid, 261, 353, 470.
 Pinacol, 142.
 Pinacolone, 143.
 Pinacols, 142, 143, 236.
 Pineapple oil, 180.
 Piperic acid, 533.
 Piperidine, 505, 507, 509.
 Piperine, 532.
 Piperonal, 533.
 Piperonylic acid, 533.
 Piperylene, 529.
 Pitch, 326, 328.
 Piuri, 591.
 Plastics, 221, 234, 240, 426, 458.
 Platinichlorides, 195.
 Polarimeter, 283.
 Polyethylene glycols, 218.
 Polygenetic dyes, 581.
 Polyhydric acids, 292.

- Polyhydric alcohols, 234, 305, 306.
Polyhydric aldehydes, 285, 305.
Polyhydric ketones, 288, 307.
Polyhydric nitriles, 294.
Polymerisation, 125.
Polyoxymethylones, 125.
Polypeptides, 546, 575.
Polysaccharides, 297, 304, 308.
Ponceau 3R, 602.
Ponceaux, 602.
Popoff's rule, 144.
Potassium acetylide, 91.
Potassium cyanate, 313, 318.
Potassium cyanide, 312.
Potassium ferricyanide, 316.
Potassium ferrocyanide, 315.
Potassium myronate, 320.
Potassium phthalimide, 459.
Potassium pyrrole, 521.
Potassium succinimide, 262.
Primary alcohols, 109.
Primary alcohols, conversion into
 secondary and tertiary, 113.
Primary amines, 195, 211.
Primuline, 605.
Procaine, 537.
Proflavine, 596.
Proline, 552.
Prontosil, 419.
Prontosil *rubrum*, 419.
Proof-spirit, 107.
Propaldehyde, 132, 139.
Propaldehyde hydrazone, 524.
Propane, 55, 61.
Propene, 86.
Propenyl acetate, 220.
Propenyl alcohol, 219.
Propenyl chlorohydrin, 222.
Propenyl dichlorohydrin, 222.
Propenylpyridine, 530.
Propenyl tribromide, 220.
Propenyl trichloride, 223.
Propenyl trinitrate, 223.
Propeptones, 575.
Propionamide, 193.
Propione, 139.
Propionic acid, 156, 166.
Propionitrile, 317.
Propionyl chloride, 161.
Propiophenone, 445.
Propylacetic acid, 156.
Propyl alcohol, 84, 110, 112.
Propylamine, 192, 211.
Propylbenzene, 363.
Propyl bromide, 68.
Propyl bromide, *iso*-, 87.
Propyl carbinol, 108, 111.
Propylene, 84, 86.
Propylene alcohol, 219.
Propylene chlorohydrin, 217.
Propylene dibromide, 84, 220.
 $\alpha\beta$ -Propylene glycol, 219, 236, 251.
 $\alpha\gamma$ -Propylene glycol, 236, 252.
Propylene oxide, 218.
Propyl formate, 173.
Propyl iodide, 70.
Propylmalonic acid, 187.
 α -Propylpiperidine, 530.
 α -Propylpyridine, 530.
Protagon, 564.
Protamine, 550.
Proteins, 543, 572.
Protocatechuic acid, 472, 533.
Protocatechuic aldehyde, 533.
Prussian blue, 316.
Prussic acid, 310.
Pschorr, 502.
Pseudo-acids, 177, 385.
Pseudocumene, 369.
Pseudocumyldiazonium chloride,
 602.
Pseudomauveine, 604.
Pseudomerism, 190.
Pseudonitrols, 177.
Pseudouric acid, 558.
Ptomaines, 545.
Purification of compounds, 3.
Purine, 559, 560.
Purine derivatives, 554, 559.
Purpurin, 498, 501.
Putrescine, 546.
Pyrazolone, 523.
Pyrazolone derivatives, 523.
Pyridine, 327, 504, 505.
Pyridine, alkaloids derived from,
 529.
Pyridinecarboxylic acids, 511.
Pyridine derivatives, isomerism of,
 507.
Pyridine-2:3-dicarboxylic acid, 511.
Pyridine-3:4-dicarboxylic acid, 512.
Pyridine, homologues of, 510.
Pyridine methiodide, 506.
Pyridinesulphonic acid, 505.
Pyridylpyrrole, 531.
Pyrogallol (pyrogallie acid), 433.
Pyrogallolcarboxylic acid, 472.
Pyrogalloldimethyl ether, 433.
Pyroligneous acid, 97, 150.
Pyromucic acid, 519.

- Pyrotartaric acid, 257, 261.
 Pyrrole, 518, **520**, 523.
 Pyrrolidine, 522.
 Pyrrolidine- α -carboxylic acid, 552.
 Pyrroline, 521.
 Pyruvic acid, **191**, 252.
 Pyruvic acid hydrazone, 191.

 Qualitative elementary analysis, 12.
 Quantitative elementary analysis, 17.
 Quaternary ammonium derivatives, 197.
 Quaternary phosphonium hydroxides, 204.
 Quinaldine, 516.
 Quinhydrone, 446.
 Quinic acid, 538.
 Quinine, 537.
 Quinine dimethiodide, 538.
 Quininic acid, 538.
 Quinizarin, 594.
 Quinol, 431, **432**, 446.
 Quinoline, 504, **513**.
 Quinoline, alkaloids derived from, 537.
 Quinoline-4-carboxylic acid, 539.
 Quinoline-2:3-dicarboxylic acid, **596**.
 Quinoline methiodide, 514.
 Quinolinic acid, 511, 512.
 Quinolinic anhydride, 512.
 Quinolsulphonic acid, 432.
 Quinone, 445.
 Quinone chloroimines, 448.
 Quinone dichlorodimines, 448.
 Quinone dioxime, 446.
 Quinone-imine dyes, 604.
 Quinone monoxime, 397, **446**.
 Quinones, **445**, 486, 496, 503, 583.

 Racemic acid, 257, 265, **276**.
 Racemic compounds, 272.
 Racemic compounds, resolution of, 278, 282.
 Racemisation, **277**, 548.
 Radicals, 74.
 Raffinose, 304.
Raoult, 38.
Rast, 40.
 Rayon, 302.
 Rectified spirit, 304.
 Reducing agents, 51.
 Reduction, catalytic, 229, 356.
Reformatsky, 213.
Reformatsky reaction, 144, 213, 263.

Reimer-Tiemann reaction, **442**, 468.
 Rennet, 577.
 Resins, synthetic, 221, 234, 240, 426, 458.
 Resolution of *dl*-compounds, **278**, 282, 545.
 Resorcin brown, 602.
 Resorcinol, **431**, 601, 602.
 Resorcin yellow, 601.
 Resorcylic acids, 467.
Rhizopus Delemar, 103.
 Rhodamines, 594.
 Rhodonates, 320.
 Rickets, 570, 571.
Riedel, 508.
Robinson, 535.
 Rocellin, 602.
 Rochelle salt, 258.
Roosen, 557.
 Rosaniline, 586, **588**.
 Rosolic acid, 590.
 Rotation, molecular, 284.
 Rotation, specific, 283.
Rouelle, 239.
 Rubber, synthetic, 324.
 Ruberythric acid, 498.
Ruff, 294.
Runge, 520.

Sabatier, 229, 357, 482.
 Saccharic acid, 277, **287**.
 Saccharimeter, 286.
 Saccharin, 455.
 Saccharomyces, 302.
 Saccharosates, 296.
 Salicin, 471, **472**.
 Salicyl alcohol, 471.
 Salicylaldehyde, **442**.
 Salicylic acid, 469.
 Saligenin, 471.
 Salipyryne, 523.
 Salmine, 550, 552.
 Salol, 471.
Sandmeyer's reaction, 376, **402**, 454.
 Saponification, 226.
 Sarcosine, **552**, 554.
 Sarkine, 560.
 Saturated compounds, 53.
 Scarlet R, 602.
Scheele, 310.
Schiff's bases, 440.
Schiff's nitrometer, 23.
Schiff's reaction, **128**, 440.
Schotten-Baumann method, 453.

- Schweinfurter green, 153.
Schweitzer's reagent, 300.
 Scurvy, 570, 571.
 Sealed tubes, 26.
 Sebacic acid, 261.
 Secondary alcohols, **109**, 209.
 Secondary amines, **196**, 211.
 Secondary aromatic bases, 395, 518.
 Semicarbazide, **241**, 563.
 Semicarbazones, 138.
 Seminin, 287.
Senderens, 357, 482.
 Separation of compounds, 3.
 Serine, 548.
 Side-chains, 355.
 Silicononane, 206.
 Silicononyl chloride, 206.
 Silicon, organic compounds of, 206.
 Silicon tetraethyl, 206.
 Silver acetylides, 91.
 Silver cyanide, **314**.
 Sinapine, 552.
 Sinigrin, 320.
 Skatole, 524.
Skraup's reaction, 513, 515.
 Soaps, 225.
 Sodium acetylides, 91, 95.
 Sodium ammonium racemate, 265.
 Sodium cyanide, 313.
 Sodium ethoxide, 103.
 Sodium glycerol, 222.
 Sodium glycol, 215.
 Sodium mercaptide, 119.
 Sodium methoxide, 99.
 Sodium nitroprusside, 316.
 Sodium phenate (phenoxide), 424.
 Sodium phenylcarbonate, 467.
 Soft soap, 226.
 Solar oil, 64.
 Solubility, 148.
 Sorbitol, **235**, 287, 289.
 Sorbose (Sorbulose), 307.
 Sorbose bacterium, 307.
 Specific rotation, 283.
 Spirit, methylated, 107.
 Spirit of wine, 101.
 Spirits, 304.
 Stannic ethyl, 211.
 Stannous ethyl, 211.
 Starch, 105, **298**, 304.
 Starch cellulose, 298.
 Starches, **284**, 304.
 Stearic acid, **158**, 166, 239.
 Stearin, 226.
 Stearone, 139, 141.
 Stereo-chemical isomerides, 271.
 Stereoisomerism, 264, 281.
 Stereoisomerism of elements other than carbon, 282.
 Stereoisomerism of unsaturated compounds, 279, 283, 465.
 Sterols, 565, 566.
 Stigmasterol, 568.
 Stilbene, 502.
 Stilbene dibromide, 502.
 Storax, 435, 463.
 Stovaine, 537.
Strecker, 552, 562.
 Strontium sucrosate, 296.
 Structure of organic compounds, 43.
 Strychnine, 539.
 Strychnine methiodide, 540.
 Sturine, 551.
 Styrene (styrolene), 358, **464**.
 Suberic acid, 261.
 Substantive dyos, 580.
 Substitution, 53, 382.
 Substitution, rules of, 382.
 Succinamide, 248.
 Succindialdehyde, 263, 521, 535.
 Succinic acid, **246**, 262.
 Succinic acid, electrolysis of, 79.
 Succinic anhydride, **247**, 262.
 Succinimide, **248**, 262.
 Succinimide, metallic derivatives of, 262.
 Succinyl chloride, 248.
 Sucramine, 455.
 Sucrosates, 296.
 Sucrose, 102, **294**, 304.
 Sugars, **284**, 304.
 Sugars, hydrazones of, 290.
 Sugars, osazones of, 290, 407.
 Sugars, synthesis of, 290.
 Sulphanilamide, 419.
 Sulphanilic acid, **419**, 601.
 Sulphates, alkyl, 177.
 Sulphides, alkyl, **118**, 434.
 Sulphobenzene stearic acid, 227.
 Sulphobenzoic acids, **455**, 471.
 Sulphocyanic acid, **319**, 321.
 Sulphonals, 120.
 Sulphonamides, 417.
 Sulphonation, 415.
 Sulphones, 119.
 Sulphonic acids, 119, 322, 354, **415**.
 Sulphonyl chlorides, 417.
 Sulphoxides, 119.
 Sulphur, detection of, 16.
 Sulphur, estimation of, 27.

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